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KEY TO ABBREVIATIONS

c — correspondence
cr — case record
e — editorial

MMS — Massachusetts Medical Society
mp — medical progress
mc — medical eponym

mr — meeting report
misc — miscellany
n — notice

o — obituary
* — original article

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CASE RECORDS
OF THE MASSACHUSETTS GENERAL HOSPITAL

WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor (on leave of absence)*
BENJAMIN CASTLEMAN, M.D., *Acting Editor*
EDITH E. PARRIS, *Assistant Editor*

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SUBACUTE DEGENERATION OF THE BRAIN IN PERNICIOUS ANEMIA*

RAYMOND D. ADAMS, M.D.,† AND CHARLES S. KUBIK, M.D.‡

BOSTON

PERNICIOUS anemia is a complicated disease that is characterized by certain changes in the blood and blood-forming organs, in the gastrointestinal tract and in the central nervous system. The primary fault is thought to be an atrophy of the gastric mucosa that induces a deficiency of certain substances essential for the maturation of red cells. The cause of the nerve-fiber degeneration is more obscure, but it has been suggested that deficiency of another factor may account for it. The most important pathologic findings are hyperplasia of the bone marrow, consisting chiefly of the less mature elements of the red-cell series, atrophy of the lingual and gastric mucosa, a variable amount of hemosiderosis in the spleen, liver and kidneys and, in many cases, degeneration of spinal white matter, especially in the posterior and lateral columns. Less well known, and in fact not even mentioned in many textbooks on neurology, are the lesions in the cerebral white matter. Because of this we feel justified in reporting the following observations in 2 cases.

Only within comparatively modern times have the neurologic aspects of pernicious anemia been fully appreciated. Although Lichtheim¹ in 1886 was the first to describe the spinal-cord pathology, Russell, Batten and Collier² in 1900 were the first to publish a full clinical and pathological description of subacute combined degeneration.

In the early part of the nineteenth century there were several references to the brain lesions of pernicious anemia in the papers of Wohlwill,³ Ransohoff,⁴ Braun,⁵ Schröder⁶ and others, but most of them were concerned with findings of dubious significance, such as petechial hemorrhages and changes in cerebral blood vessels. Preobrajensky⁷ in 1902 was one of the first to mention degeneration of cerebral white matter, but the abstract of his

paper contains such meager clinical and pathological data that the diagnoses of pernicious anemia may be questioned.

Lube⁸ in 1913 described cases of pernicious anemia in which he found miliary foci of myelin degeneration in the cerebral white matter. The lesions were said to be globular or oblong, 80 to 100 microns in diameter and closely related to blood vessels.

Barrett⁹ in 1913 reported the pathological findings in 6 psychotic patients dying of what was thought to be pernicious anemia, although in most of these cases there were not sufficient data to establish the diagnosis—according to present-day standards. Unfortunately, his material was not well adapted to clinicopathological correlation, because many of these patients had been admitted to the psychiatric ward with obvious depressions or paranoid schizophrenia long before the onset of their terminal illness. In most of them confusion and disorientation developed after the onset of the anemia. On post-mortem examination there was degeneration in the cerebral white matter in only 1 of the 6 cases; in the other 5 cases only an alteration of cortical nerve cells was thought to be present.

Pfeiffer¹⁰ in 1915 reported an unquestionable case of pernicious anemia in which mental symptoms, consisting of drowsiness, inattentiveness, confusion and disorientation, were outspoken features. Post-mortem examination disclosed, in addition to slight alteration of cortical nerve cells, degeneration of the medullated nerve fibers in the white matter of the frontal lobes.

Woltman¹¹ in 1918 reported 7 cases in all of which there were lesions in the cerebral white matter similar to those described by Lube, Barrett and Pfeiffer. His paper contains the largest series and the most complete description of the brain lesions.

Since then, although clinicians have continued to show an interest in the psychiatric aspects of this disease, as indicated by the publication of many clinical studies, the neuropathology has been neglected. Only a few scattered case reports, including those by Lurie¹² in 1919, Weimann¹³ in 1924 and Lebensart¹⁴ in 1934, have appeared in recent

*From the Neurological Unit, Boston City Hospital, the Department of Neurology, Massachusetts General Hospital, and the Department of Nervous and Mental Diseases, Harvard Medical School.

†Instructor in neurology, Harvard Medical School, lecturer in neurology, Tufts College Medical School, neuropathologist and assistant visiting neurologist, Boston City Hospital.

‡Instructor in neurology, Harvard Medical School, neuropathologist and associate neurologist, Massachusetts General Hospital.

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acid in the fasting gastric contents or after injection of histamine. The cerebrospinal fluid showed normal pressure. The total protein was 37 mg. per 100 cc., and the Wassermann reaction was negative. The urine gave a + test for albumin, and contained many white-blood cells.

The patient developed fever, tachypnea and signs of pulmonary consolidation. Following five injections of con-

Microscopic Findings

Cerebrum. Lesions were found in the central and convolutional white matter of the cerebral hemispheres, the cerebellar peduncles and, in Case 2, the optic tracts near the chiasm. The characteristic changes in the cerebrum were best demonstrated in sections stained for myelin. In these preparations the affected white matter was diffusely but unevenly pale, the unevenness being due to a more pronounced degeneration in some regions, usually around blood vessels (Figs. 1, 2, 3, 4 and 5). In many such foci, varying in size from 50 to 150 microns the myelin was completely degenerated. The axis cylinders as well as myelin sheaths were affected, though possibly not to the same extent. In the perivascular zones of more severe degeneration there were numerous macrophages filled with fat (Fig. 6). The astrocytes and oligodendrocytes were increased in number throughout the white matter, but more so just beneath the cortical gray matter than in the deeper white matter, where the myelin



FIGURE 2. *Degeneration of White Matter in the Right Occipital Lobe (Case 1 Weigert stain).*

centrated liver extract the reticulocyte count rose to 8 per cent on the 5th hospital day. Death occurred suddenly on the 8th day.

The anatomical diagnoses were pernicious anemia with subacute degeneration of the spinal cord and brain, pulmonary embolus and acute pyelonephritis.

MORBID ANATOMY

The pathological findings were so nearly alike in these 2 cases that the following description applies equally to both.

Gross Findings

Gross changes in the central nervous system were relatively inconspicuous. There was no atrophy of cerebral convolutions or enlargement of the ventricles. The leptomeninges were transparent, and the large cerebral arteries were not especially atherosclerotic. In Case 1 (after fixation in formalin) there were innumerable minute gray foci on the cut surface of the white matter, which gave it a mottled appearance. These were approximately 1 mm. in diameter and were disseminated through all parts of the centrum and corpus callosum and, to a slight degree, the convolutional white matter. No such gross changes were observed in Case 2.

On the cut surface of the spinal cord in both cases the white matter in the posterior and lateral and to a lesser extent the ventral columns was gray and translucent. These changes were most marked in the thoracic and cervical portions.



FIGURE 3. *Degeneration in Internal Capsule and Corpus Callosum (Case 2 Weigert stain)*

was more severely degenerated. The astrocytes had large cell bodies and cytoplasmic processes that were distinctly stained in Nissl preparations. The nerve cells in the cerebral cortex were not remarkable. There were no swollen cells with eccentric nuclei and chromatolysis, such as are commonly observed in pellagra and some other vitamin-deficiency diseases.

years, and in these no attempt was made to relate the mental symptoms to the brain pathology.

CASE REPORTS

CASE 1. A 54-year-old Italian woman was in good health until approximately 6 months before admission in August, 1941, to the Boston City Hospital. At first she began to tire easily and complained of paresthesia, first in the feet and legs and a few weeks later, in the hands and arms. The legs gradually became weak and finally, shortly before entry, she could not walk. She lost control of her bladder and bowels. Admission was precipitated by the acute onset of pleuritic pain, cough and fever. The patient was said to have acted queerly for the last several weeks, but it was impossible to obtain a clear account of the mental symptoms from her relatives.

On admission, the temperature was 103°F., the pulse 90, the respirations 28, and the blood pressure 130/80. The patient appeared to be in a fairly well-nourished condition.

and anisocytosis were observed in a blood smear. The icteric index was 5.0. Examination of the cerebrospinal fluid showed normal pressure and no cells. The total protein was 38 mg. per 100 cc. The gold-sol curve was 1221000000. Wassermann and Davies Hinton tests were negative. Gastric analysis showed no free hydrochloride. X-ray examination of the chest showed consolidation of the hilar portions of both lungs.

Concentrated liver extract was given parenterally in doses of 10 cc. each day for 7 successive days. Sulfathiazole was administered because of the lung findings and fever. On the 4th hospital day the reticulocytes in the blood rose to 14 per cent and on the 6th day to 22 per cent. The patient remained in a stuporous condition for several days and was only beginning to appear more alert on the 8th hospital day when she suddenly died.

The anatomical diagnoses were pernicious anemia with subacute degeneration of the spinal cord and brain, pulmonary embolus and femoral phlebothrombosis.

CASE 2. A 53-year-old Italian woman was admitted to the Massachusetts General Hospital on July 15, 1941. She



FIGURE 1. *Diffuse, Uneven Degeneration of White Matter in a Precentral Convolution (Case 2; Spielmeier stain).*

The skin and mucous membranes were pale. She was drowsy and inattentive, making no effort to respond to many of the questions asked and answering others in monosyllables. So far as could be ascertained she was not melancholic but rather apathetic. When pressed on any point, such as details of history, she became decidedly irritable. Memory for recent events was poor. She was oriented as to place and person but gave the year as 1928. The ocular movements and pupillary reflexes were normal. The tongue was red and smooth and came out in the midline without tremor. The arms could be moved but were very weak, and the legs were almost completely paralyzed. There was no atrophy of muscles. The patient was incontinent of urine and feces. Tendon reflexes could barely be elicited in the arms and were absent in the legs. The plantar reflexes were extensor in type and abdominal reflexes were absent. All forms of sensation were reduced in the arms and almost entirely absent in the legs. The only other physical findings were dullness of the chest on percussion, bronchial breath sounds and a friction rub over the base of the right lung.

The hemoglobin was 62 per cent, and the red-cell count 1,000,000. The white-cell count was 6000, with 2 per cent reticulocytes. The hematocrit was 26.9 per cent, the mean corpuscular volume 139 cubic microns, and the mean corpuscular hemoglobin content 35.9 per cent. Poikilocytosis

had had paresthesias in the legs and hands for 2 years. During the 3 months prior to admission there was progressive loss of strength in the legs and finally inability to walk. There had been precipitancy of urination and occasional incontinence. A few days before entry to the hospital she developed pain in the left flank and burning and frequency of urination. There were no remarks in the record concerning the mental status of the patient, but when admitted to another hospital a short time before, it was noted that she was vague as to details of her illness, irritable and difficult to manage. She left against the advice of the physician before a diagnosis could be made.

On admission, the temperature was 99°F., the pulse 90, the respirations 20, and the blood pressure 95/65. The patient appeared to be in a fair state of nutrition. The skin and mucous membranes were pale. Because of marked language difficulty details of mental status were not obtained. On one occasion restraint was necessary. The arm and trunk muscles were weak, and the legs were almost completely paralyzed. There was no muscular atrophy. Vibratory and position sense in the legs were absent. Tendon reflexes were absent in the legs and the plantar reflexes were extensor in type. There was incontinence of feces and urine.

The hemoglobin was 70 per cent. The red-cell count was 2,500,000 with 4 per cent reticulocytes. There was no free

ders as well as the myelin sheaths were destroyed. There was an unevenness similar to that of the brain lesions, which was more conspicuous in longitudinal than in cross sections (Fig. 8). The areas of more pronounced degeneration seemed to have no relation to blood vessels. Fat-filled macrophages were abundant. There was singularly little reaction of astrocytes, although they had increased

in our experience, do they resemble the findings observed in pellagra or the central neuritis of Meyer.¹⁵ In our cases of pellagra the columns of Goll were degenerated throughout their course as in secondary degeneration from a dorsal-root lesion; this process was not uneven as in pernicious anemia and was accompanied by a pronounced gliosis. No degeneration of cerebral white matter was observed.

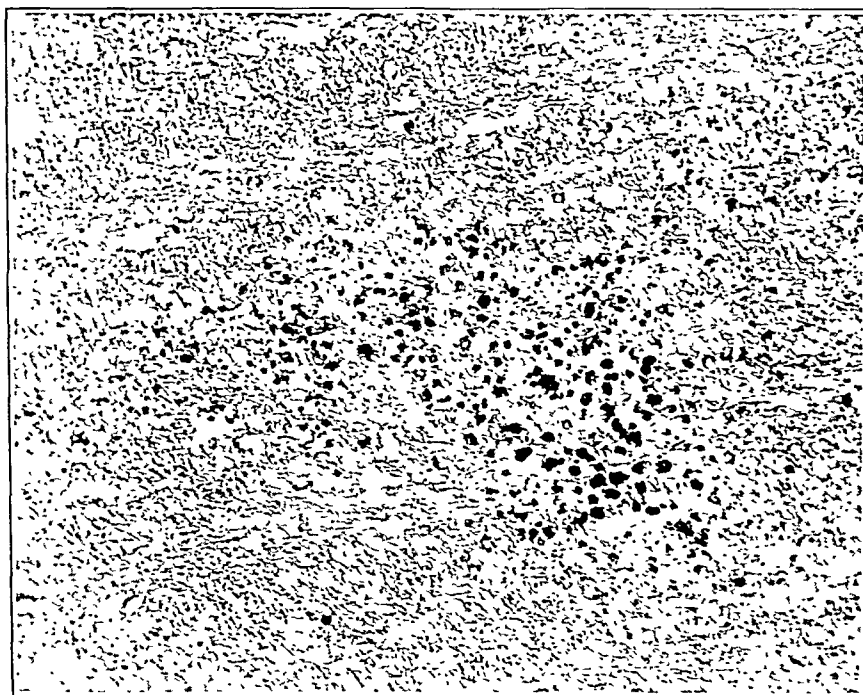


FIGURE 6. *An Area of Nerve-Fiber Degeneration (Case 1, fat stain).*
The fat in the macrophages corresponds to the distribution of the myelin degeneration.

somewhat in size and possibly in number. Nerve cells in the spinal cord were not remarkable.

DISCUSSION

Subacute Degeneration of Brain

The findings in these cases confirm the observations of others that cerebral lesions may occur in pernicious anemia. Furthermore, the cerebral and spinal-cord lesions are almost exactly alike. In both, the essential pathology consists of a more or less diffuse though uneven degeneration of the white matter, with little or no proliferation of fibrous glia. Because of this similarity it seems reasonable to suppose that this degeneration of cerebral white matter is as specifically related to pernicious anemia as is subacute combined degeneration of the spinal cord.

These changes are unique and quite unlike those that occur in cerebrovascular disorders, multiple sclerosis, Schilder's diffuse periaxial encephalitis and other more chronic degenerative diseases. Nor,

Moreover, there were swelling and central chromatolysis of the anterior-horn cells and of the larger pyramidal cells of the cerebral cortex, whereas nothing remotely resembling this was found in our cases of pernicious anemia. Although it is true that degeneration of the corticospinal tracts in pellagra has been reported by others, this too may be secondary to destruction of Betz cells in the motor cortex.

Certain authors have reported small hemorrhages and nerve-cell changes in the brain in pernicious anemia. Small, recent perivascular or capillary hemorrhages so often occur as a terminal event in many diseases that they are not of any great significance. The matter of nerve-cell changes is more difficult to assess. In some papers the descriptions are too ambiguous to permit accurate interpretation, whereas in others nonspecific changes, such as shrinkage and pigmentary atrophy, have been assigned undue importance. Where nerve-cell swelling and central chromatolysis like that of pellagra were present (Barrett,⁹ Pfeiffer¹⁰ and

Cerebellum. The Purkinje cells appeared to be normal. There were no foci of nerve fiber degeneration.

Spinal cord. The findings in both cases were identical. There was degeneration in the greater part



FIGURE 4. *High-Power View of the Myelin Degeneration Seen in Figure 1. Note the relation of the lesions to blood vessels.*

Brain stem. Nerve-fiber degeneration like that in the cerebral white matter was observed in the

of the white matter except for a narrow zone next to the central gray matter. The posterior, postero-



FIGURE 5 *Degeneration in the Optic Tract Near the Chiasm (Case 1 Weigert stain)*

middle cerebellar peduncles. The midbrain and medulla were normal.

lateral and at some levels anteromedial columns were most severely affected (Fig. 7). Axis cylin-

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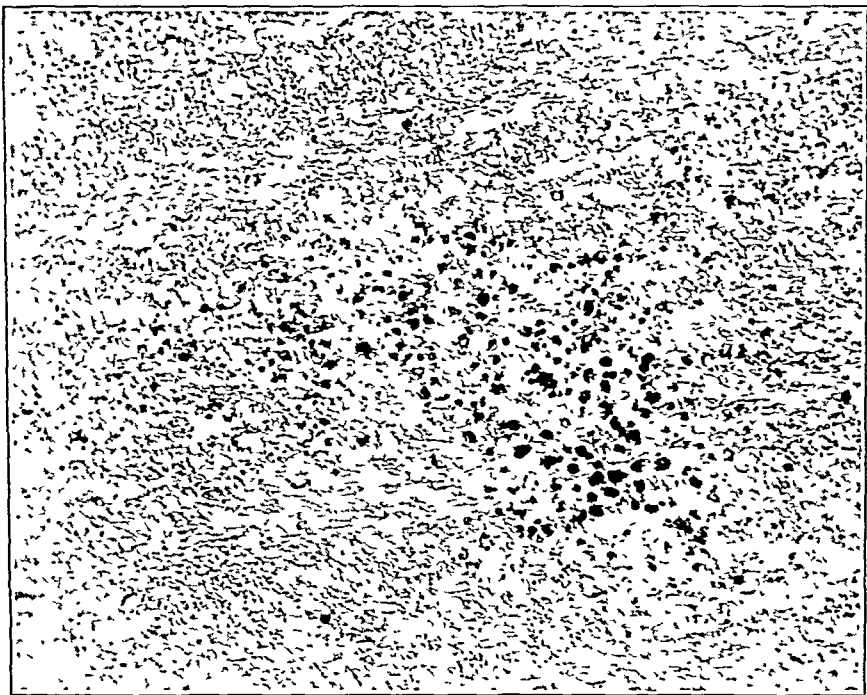


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Woltman¹¹), the possibility of associated factors such as malnutrition and vitamin B deficiency cannot be dismissed.

Relation of Subacute Degeneration of Brain to Subacute Combined Degeneration of Spinal Cord and to Pernicious Anemia

Just as degeneration of the posterior columns seems to be the initial event in subacute combined

anemia and brain and spinal-cord lesions exactly like those in our cases. In cases such as these it is obviously possible that the gastric condition bears no causal relation to pernicious anemia or subacute degeneration.

Relation between Brain Lesions and Mental Symptoms

It is a well-known fact that patients with subacute combined degeneration often exhibit mental symp-

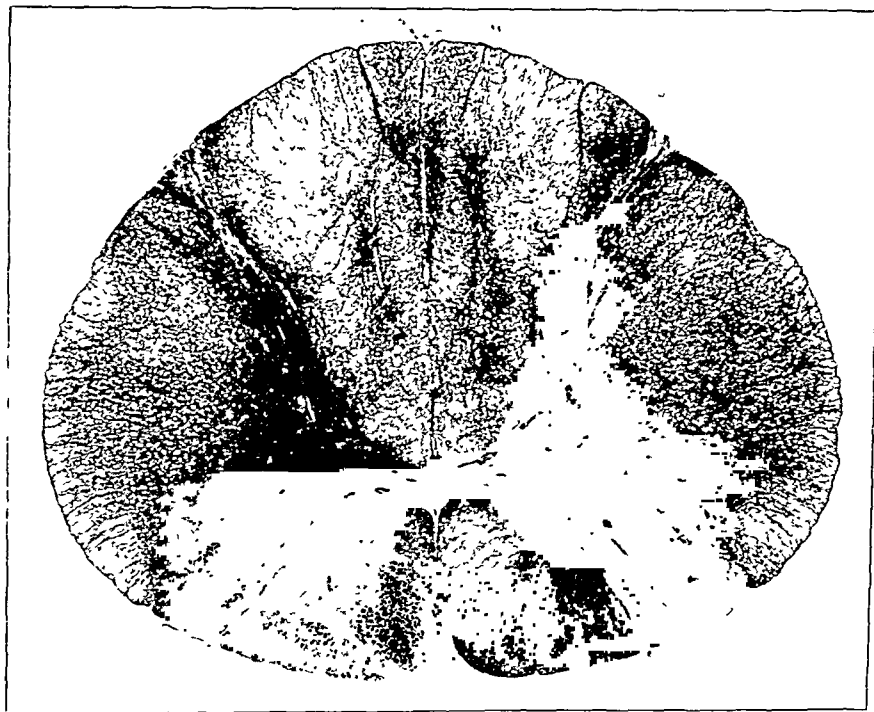


FIGURE 7. Subacute Combined Degeneration (Weigert stain).

There is an uneven degeneration of spinal white matter in the posterior, lateral and anterior columns. Note the cribriform appearance and the relative symmetry of the lesions.

degeneration, so do spinal-cord changes usually, if not invariably, precede the brain changes. Clark¹⁶ and Greenfield and O'Flynn¹⁷ have shown that the posterior columns are first affected, and that when both lateral and posterior columns are involved the oldest lesions are in the latter. In this connection, many cases have been described in which there were spinal-cord lesions without brain lesions, but in all authentic reports of subacute degeneration of the brain there have been spinal-cord lesions. Thus it seems that the order of involvement of the central nervous system is posterior columns, then lateral and anterior columns and finally cerebral white matter.

That pernicious anemia, with or without subacute combined degeneration, may develop as a consequence of carcinoma of the stomach or of gastric resection is suggested by a few carefully studied cases. Similarly, Bertrand and Ferraro¹⁸ have reported a case of gastric carcinoma with macrocytic

toms that vary from slight irritability and suspiciousness to a marked confusional psychosis. The question naturally arises as to the relation between these symptoms and the pathologic changes observed in the brain. Some writers, notably Pfeiffer,¹⁰ Barrett⁹ and Lurie,¹² affirm a causal relation, whereas Woltman¹¹ concludes that well-marked psychoses have little or nothing to do with the destroyed areas. In reviewing Woltman's case material, however, one finds mental symptoms such as irritability, mental sluggishness, fluctuation in attention and delirium in all the cases in which the mental status was recorded (Table 1).

The observation of degeneration in the optic tracts provides an explanation for reports of impaired vision by Cohen,¹⁹ Turner²⁰ and others. In our case the record gives no information concerning vision. Bickel²¹ has also reported foci of degeneration in the optic nerves of a patient with subacute combined degeneration of the spinal

TABLE 1. *Summary of Pertinent Data on Patients with Pernicious Anemia.*

CASE No	AGE	SEX	RED-CELL COUNT	HEMOGLOBIN %	COLOR INDEX	ACHLOR HADRIA	SYMPTOMS AND SIGNS		PATHOLOGY	
							SPINAL CORD	BRAIN	SPINAL CORD	BRAIN
1 (Pfeiffer ¹⁰)	55	M	0.9	30	—	+	Paresthesia, weakness of legs, sensory loss and ataxia	Drowsy and confused	Degeneration of posterior and lateral columns	Foci of myelin degeneration in cerebrum
2 (Lurie ¹²)	75	F	—	30	1.7	+	Paresthesia weakness of legs, absent tendon reflexes and Babinski sign absent	Irritable deluded and confused hallucinations (auditory), semi-comatose	Degeneration of posterior columns	Foci of nerve-fiber degeneration in cerebral white matter
3 (Lurie ¹²)	54	F	—	10	—	+	Paresthesia and ataxia, absent tendon jerks and Babinski sign	Irritable and excitable then drowsy and irrational faulty memory	Degeneration of posterior and lateral columns	Focal necrosis in medulla, pons and cerebrum
4 (Barrett ⁹)	47	M	1.5	45	—	+	Not stated	Suspicious and melancholy for 9 yr more recently auditory hallucinations, poor retentive memory and confabulation	Degeneration of posterior and lateral columns	Focal degeneration of nerve fibers in cerebrum with proliferation of macrophages
5 (Woltman ¹¹)	51	M	+	+	+	+	Aching legs girdle sensations, weakness of legs, absent tendon jerks and Babinski sign (early)	Unreasonable, irritable and stupid (late)	Degeneration of posterior, lateral and anterior columns	Myelin degeneration in cerebral white matter, medulla and cerebellum
6 (Woltman ¹¹)	42	M	1.7	47	—	+	Paresthesia increased tendon jerks Babinski sign and diminished sensation	Mental sluggishness and delirium	Not examined	Perivascular degeneration of nerve fibers in cerebrum
7 (Woltman ¹¹)	40	F	+	+	+	+	Paresthesia weakness of legs and lively tendon reflexes	Questionable mental status	+	Diffuse and focal nerve-fiber degeneration in cerebrum
8 (Woltman ¹¹)	48	M	1.0	18	—	+	Impaired sensation, Romberg sign	Marked fluctuation in attention	+	Scattered areas of myelin degeneration in cerebrum
9 (Woltman ¹¹)	51	M	2.0	50	—	+	Paresthesia ataxia and impaired sensation Babinski sign	Inattentive faulty memory depressed mood and logical thinking disordered	Degeneration of posterior and lateral columns	Degeneration of nerve fibers in occipital lobes
10 (Woltman ¹¹)	42	M	0.8	18	—	+		Delirious, talkative and restless	+	Degeneration of nerve fibers in focal areas of cerebral white matter
11 (Weimann ¹³)	55	F	—	37	1.3	+	Paresthesia incontinent sphincters ataxia and spasticity	Defective memory ideas of persecution, disoriented and demented	Posterolateral sclerosis	Focal lesions in cerebral white matter and diffuse gliosis
12 (Lebensart ¹⁴)	45	M	—	65	1.2	+	Paresthesia weakness ataxia sensory loss and plantar reflexes	Stuporous and drowsy	+	Status spongiosus in cerebral white matter with proliferation of macrophages
13 (Adams and Kubik — Case 1)	54	F	—	50	—	+	Paresthesia weakness incontinence loss of reflexes impaired sensation and Babinski sign	Confused disoriented, poor memory and stuporous semi-comatose	Degeneration of posterior, lateral and anterior columns	Focal and diffuse degeneration of nerve fibers in cerebral white matter, corpus callosum, cerebral peduncles and brain stem
14 (Adams and Kubik — Case 2)	53	F	2.5	70	—	+	Paresthesia weakness incontinence loss of tendon reflexes and Babinski sign, some sensory loss	Irritable and unreasonable, restraint because of mental confusion	Degeneration of posterior, lateral and anterior columns	Uneven degeneration of nerve fibers in cerebral white matter, optic chiasm and cerebellar peduncles

cord. In his case there were bilateral central scotomas and optic atrophy.

On the basis of these observations we favor the supposition that both subacute combined degeneration of the spinal cord and subacute degeneration of the brain represent an advanced stage in a specific process that is induced by a deficiency of certain substances necessary to the metabolism of myelinated nerve fibers. It is not to be expected that

An analysis of our cases and others indicates that patients with brain lesions have mental symptoms. The converse is not necessarily true, since cerebral lesions are not always found in cases in which mental symptoms have been present.

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FIGURE 8 Degeneration of Myelinated Fibers in a Lateral Column of the Spinal Cord (Case 2 Spielmeyer stain)

Note the resemblance between the cord lesions and the brain lesions

every patient with pernicious anemia will have demonstrable brain lesions, but all those in whom there are definite and widely disseminated brain lesions will probably have mental disorders.

SUMMARY

The clinical and pathological findings in 2 cases of pernicious anemia with subacute degeneration of the brain and spinal cord are described. In each, there were well-marked neurologic and psychiatric symptoms.

The important pathologic changes consisted of a diffuse uneven degeneration of nerve fibers in the spinal cord and cerebral white matter, with relatively little proliferation of fibrous glia. The brain lesions resembled the cord lesions so closely that there could be little doubt concerning their identity.

The pathologic process is unique and easily distinguished from that of other diseases involving the cerebral white matter and from that of pellagra.

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PART-TIME PROTECTIVE ENVIRONMENT AND WORKING PAROLE AS AN ADJUVANT IN THE TREATMENT OF ALCOHOLISM

JOSEPH THIMANN, M.D.*

BOSTON

ASIDE from other considerations, — physiologic, psychologic and sociologic, — the extremely high cost to cities, states and the federal government of the care of alcoholic patients who become a public liability has been noted so often by writers on the subject that it would be duplication to quote them at length here. The seriousness of the problem from the economic viewpoint, however, is summed up in the following statement from a paper read by Dr. Merrill Moore at the fifty-first annual meeting of the Association of Life Insurance Medical Directors of America (October 17 and 18, 1940), entitled "Alcoholism: A public health problem":

Its [alcoholism's] cost to the individual, the family and the community cannot be expressed in simple figures, for it involves such intangible and remote costs as the tax rate on your real property, the amount of money available in a tax dollar for schools and roads and the dividends which certain of your well-invested securities yield. When one reckons the cost of caring for chronic alcoholics in jails and for acute alcoholics in hospitals, the resulting figure represents only the surface cost. Persons with alcoholic psychoses increase the budget of the Massachusetts State Department of Mental Health by 10 per cent; broken homes resulting from alcoholism cause municipal and federal budgets for relief to be greatly increased; the costs incident to accidental deaths which are indirectly due to the intemperate use of alcohol are tremendous.

This is looking at the problem from the negative side. When one attempts to deal with it in a positive way, he must answer the questions, "How can this economic waste be prevented?" and "How can an alcoholic patient be helped toward physical, emotional and economic rehabilitation?" A plan that has been worked out at the Washingtonian Hospital, although it may not answer these questions fully and finally, at least seems to be a signpost indicating the way.

This is a system of working patients; that is, the patient, while still under treatment, returns to his former occupation (or finds a new job), but spends all his free time at the hospital. This arrangement has a number of advantages. The patient is in a protected environment during his free time. His evenings and nights are spent at the hospital if he

is working in the daytime or his daytime hours if he is working at night, and he is under the shelter of the hospital over week ends, a time difficult to bridge if he is living outside because of the temptation to seek the conviviality of a tavern in his loneliness and because he has nothing to do. He is, moreover, removed from the emotional instability of a home environment in which the wife or mother may have little understanding of his problem, and from the company of drinking companions. He is put on his feet financially, so that he can pay, or at least contribute to, his hospital fee and the charge for special treatment, such as the conditioned-reflex therapy. He becomes, while still under treatment, gradually more self-reliant and responsible, and self-respecting. He is in daily contact with the physician, so that psychotherapeutic interviews may help him over difficult periods.

Under this arrangement, patients whose maladjustment to life caused an acute intoxication every few weeks, with resulting inability to hold a job and be self-supporting, have worked daily and efficiently without recourse to alcohol. In some cases this has been so even before the conditioned-reflex treatment was given or psychotherapy could be expected to bear results. The patients were rid of the vicious cycle of relapses, which caused despondency and lack of faith that they would ever be abstinent, which, in turn, led again to drinking. On working parole they have gained self-confidence and self-assurance from the realization that they are being abstinent and are economically successful. Thus they grow increasingly better able to adjust to the difficulties of life, to face reality and to become poised and happy people.

CASE I. A. B., a 38-year-old Nova Scotian, who worked as a painter in a local shipyard, was admitted to the hospital in December, 1942. He was deeply intoxicated on admission, having been drinking continuously for 3 days. According to his story, he had his first drink at the age of 18 and drinking became a problem when he was 28. At the time he entered the hospital, he was drinking a quart of whisky daily and some beer and his longest period of sobriety had been 4 months. He gave as the cause of his drinking marital difficulties.

The hospital social worker was requested to interview the patient's sister and to secure a complete social history, which, in abstract, was as follows: The patient's parents were

*Medical director, Washingtonian Hospital.

natives of Nova Scotia. His father was a strict disciplinarian, a dominant person and definitely the head of the household. His mother was a mild woman, gentle and sympathetic, and there was a close tie between the patient and her. The patient was always especially interested in the mature, aggressive, masculine type of girl who is fond of sports. At the age of 26 he married a girl who was, according to the patient's sister, an aggressive, irresponsible person. There were three children by the marriage. Almost from the beginning there was much incompatibility between the patient and his wife, and after 7 years they separated. Later they became reconciled, but 4 years after the first separation they again separated and the patient went to live with his sister. Throughout the years of his marital difficulties, the patient turned frequently for help to his two sisters, who were described as fine, intelligent women with high standards but rather moralistic, repressive and critical in their attitudes.

After he had been in the hospital for 2 weeks, the patient expressed a desire to take the conditioned-reflex treatment, which was begun on December 28. The preliminary series of treatments was finished on January 5, 1943. With the assistance of the social worker, arrangements were made for the patient to return to his former place of employment on January 11. It was explained to the employer that he had come voluntarily to the Washingtonian Hospital and had been co-operative in treatment plans, and, as he had always been a good worker, his employer was willing to rehire him.

The patient was advised to live at the hospital. He was given a low rate for his board, and after he began working he assumed this obligation himself.

From February 7 until July 12, the patient had four reinforcements of the conditioning treatment. During this period, also, he was in close contact with the medical director of the hospital, the hospital social worker and the social worker at the referring agency. He earned sufficient pay to meet his hospital bills, contribute to the care of his children and pay the first installment on his income tax.

On August 16, the patient injured his ankle while at work and was transferred to a general hospital. Because this injury made climbing stairs inadvisable he could not return to the Washingtonian Hospital. He was, however, persuaded to come in for week-end stays and to make short visits to the physician during the week. He has now been totally abstinent for eighteen months.

CASE 2. C. D., a 43-year-old American citizen of Canadian birth, began drinking at the age of 17 and had never been abstinent since then. Drinking became a problem 4 years before entrance to the hospital, when he realized that he was unable to stop and that this habit was interfering with his work. He was referred to the hospital by the Court that found him guilty of drunkenness. There had been innumerable arrests for the same offense, and he had been confined at the Bridgewater State Farm six times. When drunk he was belligerent and dangerous.

According to the social history, the patient's mother had "lived for her children" and was resentful when her sons married and left her. She had been especially fond of the patient and had given him privileges that his brothers did not share. His father, on the other hand, was a severe disciplinarian and "overreligious." The patient had to leave school to go to work at the age of 13 and obtained a job as an apprentice shipwright in a local shipyard. He was a good worker and later got a job as a wood caulker, first class, at the Charlestown Navy Yard. He held this job for 5 years and then secured work at the Brooklyn Navy Yard, where he worked for 3 years. At the end of that time he returned to Boston, was re-employed at the Charlestown Navy Yard and continued to work there for 4 years. At that time his jail record commenced, and since 1939 the patient had not worked.

Meanwhile, at the age of 21, he had married a girl several years his junior. This marriage was not a happy one from the beginning, and the couple separated within a year. At the age of 26 the patient married for the second time. This wife was 9 years older than he, had been previously married and had five children. There seems to have been a strong mother-son relation in this marriage, and the patient "relied and leaned on" his wife. There were four children by this marriage.

The patient was brought into the hospital by a court probation officer on February 16, 1943. He was shabby and

unkempt, stated repeatedly that he had dragged his wife and children down to the dregs and they would be better off without him, and seemed apprehensive about being hospitalized. He was, however, anxious to have help, since he was afraid he would again be sent to Bridgewater. He was admitted for a 2-week period of observation. At the end of that time, it was suggested that he return to his job on working parole and save money to pay for the conditioned-reflex treatment. (It is believed that assuming financial responsibility by the patient as early as possible is psychologically constructive.) After working a month under this arrangement, he expressed his amazement that he could pass beer parlors and other places where liquor was sold without being tempted to go in and have a drink. He worked out a budget with the social worker and began to save toward his conditioning treatment.

On May 3, the preliminary series of treatments was begun, and to date the patient has had four preventive reinforcement conditionings. A plan was worked out whereby he gradually spent more and more of his nights at home. He was given two raises in pay.

In view of the severity of his alcoholism, this patient remained as a boarder at the hospital for a full year. He still gets easily upset over small matters, but he is being exposed gradually to the tensions that he meets outside the hospital, so that he will learn to handle them without drinking. Considering his long period of drinking and his court record, it is extremely gratifying that he continues to be abstinent after a period of 9 months.

CASE 3. A 32-year-old Irish-American had been in the hospital four times previous to his last admission in January, 1943. He began drinking when he was 22 and continued until the age of 25, when he stopped. No clear history could be elicited concerning when he resumed drinking, but his first admission to the hospital was in October, 1937. He came in again in March, 1938, in May, 1942, and in November, 1942. His attitude on each of these admissions was hostile and suspicious, and he stated that drinking was not a problem for him, since he did not drink to excess. On his fifth admission in January, 1943, however, he was more co-operative and the following social history was elicited.

The patient left school after 3 years of high school and went to work for a gasoline concern, with which he stayed for 10 years. Business later became dull and about 3 years previous to admission he got a job retreading tires. His father died when he was 10 years old and his eldest brother, who was 20 years older, seems to have taken the father's place. The patient was his mother's favorite child, and after he married at the age of 23 the mother lived with his wife and himself. His married life was harmonious until 3 or 4 years ago, when his wife's mother came to live with them. Both she and her daughter drank and arguments ensued about this, since the patient did not like to have drinking in the home. He decided that it was right for him to drink if they did, and it was shortly after this that he was admitted to the hospital for the first time. Finally he left home and took a room. Because of loneliness and worry about his child, he continued to drink. Fear that the child might be put in a "home" seemed to bring about a change in his attitude, for on his final admission he was anxious for treatment.

It was arranged that the patient should stay at the hospital on working parole, meeting his board out of his pay and saving money for the conditioned-reflex treatment. To date he has been working regularly and is entirely abstinent.

It has been found that such a protective environment should be continued for about a year, supplemented, as mentioned above, by conditioned-reflex treatment, psychotherapy, social adjustments and, if necessary, relaxation therapy. The resources of this hospital are limited. It is located in a tavern and package-store district; comfortable living quarters and adequate grounds for outdoor activities are lacking; no skillful and enthusiastic recreational therapists are available to schedule and organize the patients' free time in a pleasant way. If, in spite of all these drawbacks, constructive and

encouraging work has been accomplished, how much more could be done under more favorable conditions! With adequate grounds and resources, for instance, workshops might be set up where patients could engage in such work as carpentry, cabinetmaking, soldering and repairing mattresses, for which they would be paid a regular salary. In this way, many patients could be salvaged who had not yet reached a point in their rehabilitation where they could safely be allowed to take employment outside the hospital but would work well and efficiently if adequately safeguarded. Such patients, moreover, could be kept under treatment for an indefinite period of time, meanwhile learning a trade or becoming more adept at their own trade. When finally discharged, they would emerge from the hospital better equipped physically, mentally and economically to carry on.

Such a plan would be far superior to the present practice of sentencing an alcoholic patient to a state farm, where he works under compulsion. In sentencing a man to labor, no attempt is made to win his co-operation through an appeal to the more mature and ethical components of his personality. Such compulsory treatment of a sick person —

which an alcoholic patient really is — is likely to elicit feelings of hostility, which prevent any good effects from being achieved. In the plan outlined above, on the other hand, the patient would work on a purely voluntary basis. He would be treated as a mature, intelligent person, capable of co-operating in the plans for his rehabilitation, and his interest in helping himself would be encouraged and developed. This approach is the very keystone of successful treatment, for unless the patient's full co-operation has first been secured, the other steps in the plan of therapy — conditioned-reflex therapy, psychotherapy and social readjustments — cannot be effective.

SUMMARY

The role of a part-time protective environment with working parole (in contrast to full-time confinement) as an adjuvant to conditioned-reflex treatment and psychotherapy is discussed. According to the experience at the Washingtonian Hospital, this threefold plan represents the most promising and well-organized treatment for alcoholic patients.

41 Waltham Street

EPIDEMIC KERATOCONJUNCTIVITIS*

Report of a Case with Marked Systemic Manifestations

JOHN J. CURRY, M.D.,† AND FRANCIS C. LOWELL, M.D.‡

BOSTON

THE clinical features of epidemic keratoconjunctivitis have been well described by Hogan and Crawford¹ and more recently by Sanders and his co-workers.² According to these authors, at the onset there was usually unilateral hyperemia and swelling of the palpebral conjunctivas and "a sandy feeling" in the eye. This was associated with lacrimation, but only rarely was there a purulent discharge. After twelve to thirty-six hours the bulbar conjunctiva also became congested and hyperemic. Edema of the lids was often present in varying degrees. In a few cases pseudomembranes appeared, usually on the conjunctiva of the lower lid. Corneal infiltration appeared in 52 per cent of Sanders's series of 80 cases, and in 33 per cent of these was associated with 5 to 15 per cent impairment of vision. In 42 per cent of the series the other eye became involved after varying periods of time. Swelling of the preauricular glands was found in 93 per cent of the cases, and considerable significance was attached to this finding.

Among the systemic manifestations headache was by far the most frequent, appearing in 61 per cent of the cases. As a rule it was moderately severe and not relieved by analgesics. Fever and malaise were also noted.

It appeared that trauma or inflammation might predispose the eye to an attack of epidemic keratoconjunctivitis. The possibility of transmission by means of instruments and solutions used in eye examinations in the New York epidemic was also mentioned.

The sequence of appearance of the objective signs and their intensity varied greatly in the cases studied. The initial symptoms had no bearing on the duration or severity of the disease.

The following case is reported because it had many of the features of epidemic keratoconjunctivitis in association with prominent systemic manifestations. An opportunity was afforded for hospital study, which revealed the presence of abnormal lymphocytes in the blood, with a marked fall in polymorphonuclear cells during convalescence, a palpable spleen and a normal spinal fluid. Antibody for the virus of epidemic keratoconjunctivitis appeared in the serum after recovery.

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Instructor in medicine, Boston University School of Medicine; chief resident, Evans Memorial, Massachusetts Memorial Hospitals.

‡Assistant professor of medicine, Boston University School of Medicine; member of staff, Evans Memorial, Massachusetts Memorial Hospitals.

CASE REPORT

W.M., a 27-year-old, married metal worker, was admitted to the Massachusetts Memorial Hospitals on February 4, 1943, because of severe frontal and occipital headache associated with fever of 5 days' duration. He had previously been well except for a mild respiratory infection that cleared completely 14 days before the onset of the present illness. One week before admission he had a chilly sensation followed by fever, which subsided by evening. Fever recurred the following morning, and at that time he noted swelling about his eyes, which became quite painful. Lacrimation was profuse. The lymph nodes in the region of the ears were enlarged and tender. Frontal and occipital headaches appeared and quickly became severe. Salicylates failed to give relief. With an increase in fever, sulfathiazole was given in therapeutic amounts. This produced no change in the patient's condition, and the drug was discontinued after 3 days.

The red-cell count was 4,500,000 and the hemoglobin 12.5 gm. per 100 cc. The white-cell count was 6800, with 76 per cent neutrophils, 18 per cent lymphocytes, some of which were atypical, 5 per cent monocytes and 1 per cent eosinophils. The urine was normal on several examinations. The Hinton test on the blood serum gave a negative reaction. The blood nonprotein nitrogen was 21 mg. per 100 cc., and the fasting blood sugar 81 mg. The total protein of the blood was 6.09 gm. per 100 cc., with the albumin and globulin fraction 2.63 and 3.46 gm., respectively. Several cultures of the throat, eyes and blood failed to show any pathogenic organisms. Repeated agglutination tests on the blood serum for typhoid, paratyphoid, typhus and undulant fevers and dysentery were negative. The blood sulfathiazole level was zero.

The course in the hospital is shown in Figure 1, in which the major features of the illness are correlated. Shortly after entry the patient was placed in a darkened room and strictly

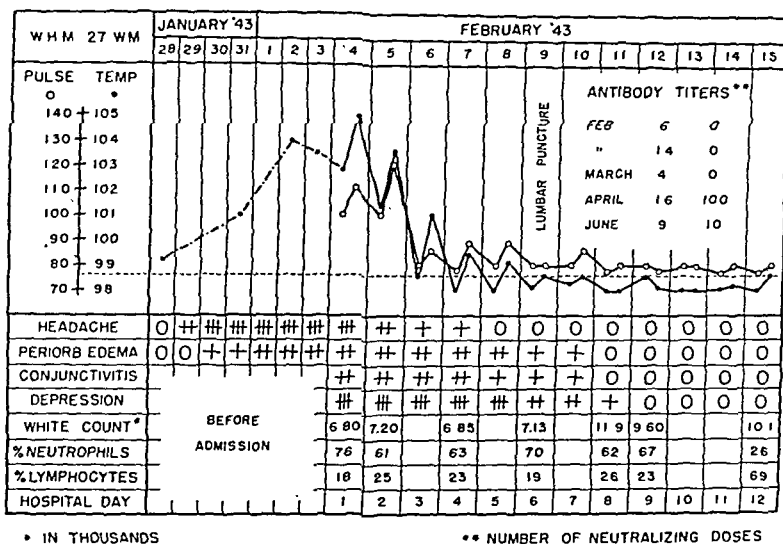


FIGURE 1. Chart Showing Clinical Data.

At that time the temperature was 103.5°F. The following morning he was referred to the hospital for treatment.

The patient stated that he had had foreign bodies in his eyes on several occasions, since his work entailed frequent grinding of metals, the most recent occurrence of this kind having been 2 months before the present illness. One week prior to its onset a fellow employee had a "sore eye" due to a foreign body. In common with other employees the patient had been working longer hours than usual and under increased tension.

On admission the rectal temperature was 101.8°F., the pulse 100, the respirations 20, and the blood pressure 122/80.

The patient was well developed and well nourished. Lethargy was pronounced. There were several evanescent zones of erythema scattered over the face and forearms. Periorbital edema was moderate, but especially pronounced in the upper lids, particularly on the right. The conjunctivas were diffusely injected. There were no follicles, hemorrhages or pseudomembranes. Photophobia was marked and lacrimation was profuse. There was no purulent discharge. Vision on gross tests was unimpaired. The cornea and fundi were normal, and no evidence of keratitis was found. The oral mucous membranes were hyperemic, with several herpetic lesions on the anterior fauces and palate. There were enlarged, tender lymph nodes in the preauricular, occipital and cervical regions and in the right axilla, and there were nontender nodes in both inguinal regions. No other lymph nodes were palpable, and the neck was not stiff. The heart and lungs were normal and the abdomen was soft. The liver and spleen were not palpable. There was no edema except that noted in the orbital regions. Neurologic examination was normal except for the presence of slightly increased bilateral reflexes.

isolated. On the 1st and 2nd days he voided large amounts of urine at infrequent intervals. During that time the erythema of the skin and the herpetic lesions in the oral cavity disappeared. For the first 4 days there was a gradual fall in temperature and the headache decreased, but lethargy, periorbital edema and conjunctivitis persisted. Treatment was symptomatic. Cold boric compresses were applied to the eyes, and codeine and aspirin were given for the headache.

X-ray examination of the chest on the 2nd day revealed perihilar and peribronchial infiltration, and little change was noted when the examination was repeated on the 7th day. By the 5th day the headache had disappeared, but because of persistent depression a lumbar puncture was done. It yielded a clear colorless fluid. The initial pressure was 165 mm. of water, the dynamics were normal, and there were 4 lymphocytes per cubic millimeter. The total protein was 51 mg. per 100 cc., the sugar 80 mg., and the chloride 691 mg. A Wassermann test and colloidal-gold test were negative. The next day the temperature was normal and the spleen became palpable for the first time. The corrected sedimentation rate was 0.7 mm. per minute. The heterophile agglutination test with a dilution of 1:64 was faintly positive. X-ray films of the skull and a flat plate of the abdomen were negative. On the 9th hospital day the patient was allowed up, and 3 days later he left the hospital.

During the hospital stay and following discharge samples of blood serum were collected for antibody determinations (Fig. 1). No antibody was demonstrated during the acute phase of the illness.* A significant titer of antibody was present in the specimen taken 2 months after discharge. No antibody against the Eastern and Western strains of equine

*We are indebted to Dr. Murray Sanders for the antibody determinations, which were carried out in his laboratory at Columbia University.

encephalomyelitis was found. In view of the herpetic lesions on the roof of the mouth, noted on admission, it is perhaps unfortunate that tests for antibody against the herpes virus were not carried out. The clinical course and the short duration of these lesions do not, however, lend support to the view that the herpes virus played a dominant role in the patient's illness.

COMMENT

The diagnosis of epidemic keratoconjunctivitis is easily made in the presence of an epidemic and when conjunctivitis and periorbital edema on one or both sides, enlargement and tenderness of the preauricular lymph nodes and keratitis are found. When keratitis is absent, as it is in 47 per cent of the cases,² and the disease is sporadic, the diagnosis is difficult unless the virus of epidemic keratoconjunctivitis is isolated or a rise and fall in antibody titer is demonstrated after the acute phase of the illness.³

In the present case, keratitis was absent and isolation of the virus was not attempted. Antibody in low titer did, however, make its appearance after recovery, which gives support to the clinical impression of epidemic keratoconjunctivitis. The possibility cannot be ruled out that the patient had some other virus infection that was followed by an antibody response demonstrable by the technic used.

Trichinosis and acute glomerulonephritis were considered on entry, but nothing in the clinical course supported these diagnoses. The presence of atypical lymphocytes and a palpable spleen suggested infectious mononucleosis, but the atypical cells were not the type usually seen in this disease, and furthermore the heterophile agglutination test seven days after admission—fourteen days after onset of the illness—was only faintly positive in a dilution of 1:64, a result that is considered to be within normal limits.

The history of exposure to a fellow employee who had a "sore eye" one week before the onset of the patient's illness is of interest because it coincides

with the probable incubation period of epidemic keratoconjunctivitis which is believed to be seven to ten days.

The marked depression with only mild ocular disease is unusual. Two cases were noted in the Schenectady epidemic.⁴ One case showed persistent marked sleepiness, and in both cases severe emotional disturbances were present. As shown by Figure 1, the depression was not only severer than the ocular disease but also cleared less rapidly.

The rise in antibody was unusually delayed. No antibody was demonstrated in the blood obtained one month after recovery. One month later, however, a titer of 100 neutralizing doses was present. Four months after recovery this had fallen to 10 neutralizing doses. In the studies reported by Sanders and Alexander³ the antibody titers in the blood of patients recovering from epidemic keratoconjunctivitis varied between 100 and 10,000 neutralizing doses, and in a few cases the titer has been even higher.⁵

SUMMARY

A case is presented that showed many of the signs and symptoms of epidemic keratoconjunctivitis.

The outstanding feature was the presence of severe depression with only mild ocular disease.

Serologic studies during convalescence showed the development of antibody against the virus of epidemic keratoconjunctivitis.

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MEDICAL PROGRESS

THE PHYSIOLOGIC SIGNIFICANCE OF VITAMIN C IN MAN*

LIEUTENANT MICHEL PIJOAN (MC), U.S.N.R., AND
LIEUTENANT-COMMANDER EUGENE L. LOZNER (MC), U.S.N.R.

BETHESDA, MARYLAND

FOR hundreds of years seafaring men experienced the ravages of scurvy. At the time of Columbus, scurvy was one of the most prevalent diseases of Europe. In fact, many observers thought that most diseases could be considered as outgrowths of scurvy. The medical literature is vague in reporting the first cases, but the disease was known as a most serious affliction among the Crusaders. Toward the end of the fifteenth century, Vasco da Gama reported that on his voyage around the Cape of Good Hope scurvy took by death nearly two thirds of his crew. In 1535, Cartier in Canada lost a quarter of his men by scurvy and the rest were rendered somewhat incapable by it. From the natives it was learned that decoctions from leaves and twigs served to cure or ameliorate the disease. Captain Cook and his men, on the other hand, escaped scurvy, as he reports, by provisioning their ships with fresh fruits from each shore they visited. The important feature of most naval medicine in the eighteenth century was the subject of scurvy, and in 1785 Sir Gilbert Blaine recommended lime juice in his *Observations on the Diseases of Seamen*, and thus the sailors were shortly nicknamed "limies." In 1841, Budd explicitly ascribed the antiscorbutic property of certain foods to a "definite substance," which, he wrote, "it is hardly too sanguine to state, will be discovered by organic chemistry or by the experiments of physiologists in a not too distant future." Some ninety years later his prediction was fulfilled. Thus today it is not strange that the problems of scurvy and the vitamin specifically involved in preventing this disease should receive attention.

Within the last ten years a voluminous literature has accumulated on sundry subjects containing the words "ascorbic acid" as the only common denominator. In fact, the current rate for such publications in the *Index Medicus* exceeds three hundred annually. Two forces appear to be responsible for the ascorbic acid miscellanea: first, the isolation and synthesis of the vitamin, and second, the development of methods for its assay. Despite the care and the delicacy required by the latter analytical procedures, they have been responsible for more than 75 per cent of the current literature

on this subject. A study of this stream of publications reveals, furthermore, that with no conceivable regard to any relation to the scorbutic process, vitamin C and its laboratory evaluation have been employed in almost every phase of normal and diseased body economy.

During the last three years, Butler andushman,^{1,2} Crandon, Lund and Dill³ and Rietschel and Mensching⁴ have contributed critical investigations on ascorbic acid deficiency. In the light of their investigations, the present communication reviews the function of ascorbic acid in body economy and presents additional observations bearing on the laboratory evaluation of vitamin C deficiency and on the human requirements of this acid. Two theses will be proposed and examined: that the only known lesion caused by vitamin C deficiency is the scorbutic process⁵; and that the evaluation of ascorbic acid deficiency in any given person from an assay of his usual diet is untrustworthy.

From the first proposition, it follows that ascorbic acid — whether synthetic or derived from food — has but two known uses, the prevention and the treatment of scurvy. The possible exception of its action in the intermediary metabolism of aromatic amino acids in premature infants^{6,7} is interesting and requires further investigation. Any other use of the vitamin in man lacks controlled experimental justification.

As regards the second proposition, not until a diet can be shown to produce a steady linear decline in the vitamin C content of the white cell-platelet layer or whole blood or to produce scurvy is one justified in calling the diet deficient. Inasmuch as scurvy can be anticipated only when the cellular elements of the blood become depleted of vitamin C, the level in cell-free plasma becomes an unreliable index. The ability to maintain a fixed level of vitamin C in the plasma, no matter how small, indicates for the person concerned a positive ascorbic acid economy.

ASCORBIC ACID

The discovery in 1907 by Holst^{8,9} that guinea pigs developed a deficiency disease distinct from polyneuritis and similar to human scurvy soon aroused the interest of chemists. Inasmuch as for centuries citrus fruits had been known as prophylactic and therapeutic agents against scurvy, the

*From the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland.

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newer studies began with concentration and isolation experiments, using lemon juice. The lack of stability of the vitamin hampered its immediate isolation, but a few properties of the antiscorbutic agent were recognized, including the fact that the active principle is destroyed by oxygen and tends to be more stable in acid solutions.¹⁰ Furthermore, it was observed that all biologic fluids capable of antiscorbutic action possess the common property of reducing a number of reagents.¹¹ On this basis, chemical methods were attempted to assay the antiscorbutic quality of foods. In the main, the early methods proved unsatisfactory. In 1930, it was found that the redox dye,^{3,7} dichlorobenzene indophenol, is particularly sensitive to reduction by some substance (reductone) having antiscorbutic properties.¹² In fact, there appeared to be a direct relation between the antiscorbutic property of a biologic fluid and its ability to reduce the redox dye. Final proof of this relation had to await the isolation of the vitamin and the eventual critical tests to which an assay must inevitably be subjected.

Following the isolation of the vitamin by King and Waugh^{13, 14} in 1932 and its identification with Szent-Györgyi's hexuronic acid,^{15, 16} it was soon synthesized from precursors having no antiscorbutic properties.¹⁷⁻¹⁹ The synthetic vitamin proved to be specifically antiscorbutic and reduced the redox dye, 2,6-dichlorobenzene indophenol, in equivalent molar concentrations. Thus, the claim for the dye method of assay, except in its complication by other reducing and interfering substances, was substantiated. It was shown, furthermore, that the levorotatory form, and not the dextrorotatory form, is antiscorbutic. The vitamin when in solution was unstable, — a finding previously noted concerning antiscorbutic biologic fluids, — oxidation being responsible for this instability.

Crystallographic and x-ray measurements of crystallized ascorbic acid (molecular weight 176) show that the molecule is flat.²⁰ It is soluble in water (1 gm. dissolves in 3 cc.), less soluble in alcohol (1 gm. dissolves in 50 cc.) and insoluble in benzene, ether, chloroform and fats. Since it is relatively unstable, such catalysts as traces of silver, copper and light — especially in the presence of riboflavin²¹ — must be avoided. The oxidation potential (E_0) of ascorbic acid at pH 4 at 35°C. is 0.166 V.²² In solution, vitamin C exhibits acidic properties, having a pK_1 of 4.17 and a pK_2 of 11.57. It has a typical ultraviolet absorption spectrum with a maximum at 265 μ . When ascorbic acid reacts with the redox dye, 2,6-dichlorobenzene indophenol (molecular weight 290), two enolic hydrogens of the ascorbic acid molecule reduce 1 molecule of dye. In the assay of the vitamin in biologic fluids the errors due to interfering substances, turbidity, extraneous pigments and oxidation can in the main be circumvented by special technic,²³⁻²⁶ and it is these techniques that are recom-

mended. A recently introduced method²⁷ shows considerable promise. By this method the ascorbic acid present is converted to dehydroascorbic acid, and on treatment with 2,4-dinitrophenylhydrazine an osazone is formed. In fact, it appears to be more trustworthy than the method using redox dye for whole-blood or tissue assays,²⁸ since hemochromogens and RSH compounds interfere with the accuracy of the redox system. In foods the phenylhydrazine method of assay requires considerable care, since osazones may form from substances other than ascorbic acid.

Recently the photochemical method for the determination of ascorbate with methylene blue has been applied and has been found more accurate and specific for small samples of blood than the commonly used dichlorobenzene redox.²⁹ In fact, this method makes the accurate assay of the vitamin C in 0.2 cc. of capillary blood an acceptable clinical procedure.

Although chemical and to some extent physical methods are replacing the biologic method of assay, the latter retains its place as the ultimate and definitional method of determining antiscorbutic activity. The biologic procedure, using guinea pigs, has been well established.^{30, 31}

THE SCORBUTIC PROCESS

The prolonged lack of sufficient ascorbic acid in the dietary produces in man, primates and guinea pigs a condition known as scurvy. It is assumed with good evidence that the other animals must be capable of synthesizing a part of or all of their requirements,³² since ascorbic acid is found in about the same proportion in their tissues. Furthermore, these other animals fail to exhibit the scorbutic process. At no time during the life cycle of man, however, is it known that synthesis of ascorbic acid takes place.³²

The scorbutic process is dependent on the depletion of ascorbic acid in animal tissues and the resultant morphologic change in the intercellular substance of certain mesenchymal derivatives.³³

In the scorbutic animal the ground substance, and fibroblasts are present as in the healthy animal, but collagen is not formed.³³ When the defective animal is given ascorbic acid, however, the condition is corrected and translucent bundles of collagen quickly appear.³⁴ The exact mechanism by which ascorbic acid effects this dramatic change is not known. The intercellular substance of bone (osteoid tissue) and of teeth (dentine) may be similarly affected by withdrawing or administering ascorbic acid. In scurvy all tissues lose collagen. Just where the weakness occurs in blood vessels is not known. Whether it develops in the sheath or in the endothelial cement substance, the fact remains that the vessels become more fragile and rupture easily on application of trauma or even do so spontaneously. As a result, hemorrhages occur, there is a fragmen-

tation of muscle fibers, and an intense reparative effort is apparent by the striking multiplication of sarcolemma. The gums, lacking cement substance, become boggy and swollen; infections may occur that often develop into pyorrhea. The more the gums are traumatized by chewing and so forth, the more serious this manifestation becomes.

Thus it is seen that stress modifies and to some degree determines the site of the gross lesions. The pressure of boots, the rubbing of trousers,³⁵ the location of vessels near a bony prominence and so forth are of considerable importance in explaining the distribution of the lesions. Blacksmiths and carpenters in times past developed lesions in their shoulders and arms; soldiers, in the calf and lumbosacral muscles.³⁶ Petechial hemorrhages of the eyelids are not uncommon in this disease, and perifollicular hemorrhages are an early sign. Lesions are further modified by growth. For instance, in infants bone changes are most striking, but in adults they are almost entirely lacking. In the latter, however, the dentine undergoes fairly rapid resorption and porosis.

Multiple periosteal hematomas become less and less frequent as the age of the patient increases; it is in the young and growing animal that bone pains chiefly occur. Hemorrhages in the muscles and joints may play a considerable role in the production of such pains. Other lesions include blood-stained effusions into the body cavities, which may give rise to bloody diarrhea. Lesions may at times be complicated by other diseases.³⁷⁻³⁹

Enlargement of the heart has been noted in a few cases of scurvy, and circulatory collapse has been described. Thiamine deficiency may contribute to such changes.

Clinically the scorbutic manifestations are often mixed with other nutritional deficiencies and the picture may be somewhat modified. Aside from other vitamin deficiencies superimposed on scurvy, prominent is the anemia that is often associated with it. Much has been written relating this anemia to a specific hemopoietic need for vitamin C.⁴⁰ Recent work, however, tends to disprove this, and the anemia seems to be frequently related to blood loss and to be relieved by iron therapy alone.⁴¹

PHYSIOLOGIC RELATIONS

The established role of ascorbic acid in animal tissues lies in its relation to intercellular material. In this relation the vitamin participates indirectly in calcium metabolism. Thus, in scurvy the osteoblasts, unable to form osteoid tissue, revert to a prototype and attempt to form a fibrous union between diaphysis and epiphysis.⁴² The chemical mechanism by which this vitamin induces the formation of collagen is unknown.

Many investigations have been presented in an endeavor to determine the subtle mechanisms of the

action of vitamin C. These investigations are in the main fortuitous observations in vitro and have little or no significance in vivo. For instance, it is known that ascorbic acid and dehydroascorbic acid and a number of their cation complexes (Fe^{++} , Cu^{++} and Mn^{++}) exert an effect on specific enzymes, such as cathepsin, papain, amylase and urease.²¹ The results from different laboratories are not in agreement, and it is probable that the conditions of experiments were not similar.

The catalyst found in many plant tissues capable of oxidizing ascorbic acid to dehydroascorbic acid and called "ascorbic acid oxidase" is a protein-copper complex.⁴³ Since there is evidence that the enzyme is not specific for ascorbic acid as a substrate, the above name should be used only in a restricted sense. In animal tissues, on the other hand, cytochrome-indophenol oxidase acts as the catalyst.⁴⁴ Hemochromogens likewise have a direct effect on ascorbic acid. It should be borne in mind that the role of all these mechanisms in the living animal is unknown.

The theory that ascorbic acid acts as a hydrogen transport or a respiratory catalyst in relation to animal tissues is unacceptable because there is no clear-cut evidence supporting this view.⁴⁵ Tissues depleted of ascorbic acid do not show a decreased respiration capacity, and when ascorbate is added to the depleted tissues, there is no rise in true oxygen consumption.

Recent unconfirmed reports suggest that ascorbic acid acts as an inhibitor in the adrenalin-adrenochrome oxidation in heart tissue.²¹ The effect of ascorbic acid and guinea-pig complement is interesting but has not been demonstrated conclusively in man. Thus, to date the chief role of ascorbic acid in human beings remains that of maintaining sufficient intercellular substance, and the lack of it results in the scorbutic process.

VITAMIN C DEFICIENCY AND ITS RELATION TO HUMAN REQUIREMENTS

Fundamentally, in the light of the foregoing, the amount of ascorbic acid needed in the body is that required to prevent scurvy. During recent years a great deal has been written with reference to the ascorbic acid status of normal and diseased persons. In the main, these investigations fall into three groups: those that deal with plasma levels of ascorbic acid as a reflection of the dietary intake, those that deal with plasma levels as a reflection of the tissue content of the vitamin and those that deal with ascorbic acid in terms of body saturation. By these methods a galaxy of nonscorbutic conditions have been studied. Such terms as "a relative insufficiency" of ascorbic acid, "subclinical scurvy" and the ascorbic acid required for "optimum health" are essentially undefined; the use of the term "latent scurvy" as a clinical entity described by Hess⁴⁶ is probably acceptable.

Significance of Blood Levels of Ascorbic Acid

The question of the meaning of blood values has recently been answered almost completely by a direct and well-planned experiment. Crandon³ conceived the idea of inducing scurvy by placing himself on a vitamin C-free diet and studying the changes that occurred in the process. His ascorbic acid plasma level dropped to zero within forty-one days and remained there for a period of thirteen weeks before the signs of scurvy appeared. On the other hand, the white cell-platelet layer fell to zero just prior to the advent of the first signs of scurvy.

Butler and Cushman^{1,2} had already observed that the ascorbic acid content of the white cell-platelet layer of centrifuged blood is probably the most accurate indicator of prescorbutic status. These investigators found that this level may be well within normal limits (25 to 38 mg. per 100 gm.), in spite of a very low plasma level. These cells apparently represent actual tissue stores of this vitamin. Thus, low plasma values do not necessarily indicate a scorbutic process unless such values exist concomitantly with a deficiency of the white cell-platelet content.

It appears from these studies that a fixed plasma value, no matter how low provided some is present, indicates a positive ascorbic acid economy. A continued drop in the plasma values and, of even greater importance, that in the white cell-platelet values indicate a shortage of the vitamin in the dietary.

There is no clinical justification for the idea that a plasma level above 0.7 mg. per 100 cc. is necessary for optimum health.⁴⁷⁻⁴⁹ One of us (M. P.⁵⁰), when studying a group of Indians whose dietary pattern was fairly rigid both in summer and winter seasons, assumed that a low plasma value implies an insufficiency of ascorbic acid. In spite of the fact that during winter months the daily intake of ascorbic acid failed to exceed 15 mg., no case of frank clinical scurvy could be found. It was believed, however, that probably a mild scurvy existed, a misconception that is now acknowledged. In a later study of early Spanish-American settlers stigmas of scurvy on dietaries never exceeding 25 mg. of ascorbic acid daily could not be ascertained.⁵¹ It was thought that for some obscure reason that had eluded most investigators, a continued low intake of ascorbic acid did not produce symptoms of frank scurvy. Thus, in the light of these studies there is no reason to presume, as some have indicated,⁵² that a level of 0.5 mg. per 100 cc. or less is diagnostic of scurvy. Ingalls⁵³ pointed out some time ago that in scurvy the plasma ascorbic acid values are always zero or a titratable trace within the error of the method. Crandon, Lund and Dill³ clearly demonstrated that a plasma level of zero content, provided that the white cell-platelet vitamin content is sufficient, produces no untoward physiologic effects.

The findings of Rietschel and Mensching⁴ are entirely confirmatory. They placed a normal man on a vitamin C-free diet for one hundred days. The plasma level and urinary excretion fell to zero, but no evidence of scurvy, capillary fragility or physiologic defect and no clinical symptoms appeared. It is only when the white cell-platelet layer falls significantly that certain symptoms manifest themselves and scurvy is expected.^{1,2} Crandon's experiment showed that the white cell-platelet level of ascorbic acid is the last to be depleted in experimental scurvy and the first to reach its peak following therapy.

The whole-blood value, indicating a combination of what exists in the plasma, the red cells and particularly the white cell-platelet layer, is also a better index than is the level in cell-free plasma,^{1,2} and falls gradually on a scorbutic diet until such time as the traces of ascorbic acid in the white cells and platelets are sufficiently low to be unmeasurable when diluted by the plasma and red cells.

In summarizing the blood values of ascorbic acid, it can be said that a steady depletion or continued lowering of the plasma value and subsequently the white cell-platelet layer indicates a dietary shortage, and that when the white cell-platelet layer levels become completely depleted scurvy follows.

It should be emphasized that the diagnosis of scurvy without clinical signs, solely on the basis of laboratory procedures, can never be justified. On the other hand, a prescorbutic state based on depleted white cell-platelet values as an index is warranted because it is during this period that Crandon noted fatigue and weakness as well as certain other changes.

Since Crandon's experiment, one of us (M.P.) has maintained a plasma value of 0.0 to 0.2 mg. of ascorbic acid per 100 cc. of plasma with no untoward signs of symptoms (see the section on wound healing below). This has lasted for twenty months, and the white cell-platelet value has been remarkably constant at 26 ± 2 mg. per 100 gm. of cells. At no time has there been evidence of any urinary excretion of ascorbic acid.

It appears at once from the above that what is important in the evaluation of the ascorbic acid status is the tissue ascorbic acid value, which is best represented for test by a whole-blood or a white cell-platelet determination. It may be conjectured that the plasma level indicates essentially an overflow or a phase of positive balance, and that when this becomes high enough urinary excretion takes place.⁵⁴

Unlike many of the other vitamins in man, ascorbic acid requires a constant intake to maintain a fixed tissue level. If one is well supplied with vitamin C (presumable saturation), he may be able to go for many months without the vitamin until the continued linear decline in the tissues reaches

zero. On the other hand, certain maintenance doses protect from scurvy.⁵¹ At present there is no clear-cut way of determining whether body economy is more effective under saturation or under unsaturation while a positive balance is maintained. Nevertheless, it must be realized that 16 to 25 mg. of ascorbic acid daily protects the human subject against scurvy. The saturation test has little or no bearing on the subject of frank clinical scurvy.

In this regard it is interesting to note that although infants are extremely susceptible to scurvy, they fail to develop it on fresh cow's or mother's milk.⁴⁶ On the other hand, processed milk does not protect against scurvy.⁴⁶ With this in mind, reference is made to the careful observations made in 1915 by Still,⁵⁵ who showed that nearly 80 per cent of the cases of scurvy appeared between the ages of six and ten months and that the disease required from six to nine months to become manifest, depending on the degree of dietary deficiency. It is evident, therefore, that there must be a prolonged period of nutritional failure that precedes the diagnosis. It is apparent that different degrees of tissue saturation determine the time interval required for scurvy to manifest itself during a dietary deficiency. For instance, in the past it had been noted that among soldiers and sailors a certain number developed scurvy on a ration that did not harm others. These observations may be of importance during present times, when members of our armed forces may be given large doses of the vitamin — a total of 3 or 4 gm. over a few days — before undergoing missions during which the intake or source of vitamin C may be limited. On the whole, however, the general thesis remains that relatively small amounts of ascorbic acid are required in the dietary to prevent scurvy in man. In monkeys the requirements are sometimes greater, and the guinea pig in terms of body weight requires more ascorbic acid than does man.

Contrary to this point of view are the opinions of others. Intakes of ascorbic acid as high as 60 to 100 mg. or even more a day have been recommended.⁵⁶⁻⁵⁸ The reason for the high intake is based on saturation results, in which a high intake is required to maintain a daily excretion of ascorbic acid approximating the amount ingested. A high intake for a short period of time may be advantageous only when a dietary shortage is contemplated or anticipated.

Significance of Urinary-Excretion and Saturation Tests

In 1935, Abbasy, Harris, Ray and Marrack⁵⁹ introduced the determination of the twenty-four-hour urinary excretion of ascorbic acid as an index of the status of this vitamin. They assumed that a low excretion level indicated an insufficiency. It was soon found that this method was unsatis-

factory,⁶⁰ because of the wide variation in excretion and the poor correlation with plasma values.

The saturation test soon replaced the urinary-excretion test in the evaluation of ascorbic acid status. This involved the administration of fairly large doses of ascorbic acid and the assay of this vitamin in the urine. Johnson and Zilva⁶¹ believed that saturation of the tissues with vitamin C was reached when the quantity ingested approximated the daily excretion. Aside from the fact that other reducing substances may be present in the urine and the fact that the kidney reabsorbs about all the ascorbic acid excreted unless complete saturation is present, the test has numerous faults. First of all, Hawley, et al.⁶² report that the amount of ascorbic acid excreted in the urine may vary according to the acid-alkaline content of the diet, and others⁶³ have reported changes in urinary excretion following the administration of various preparations. Furthermore, on the basis of Crandon's³ experiment the assumption that saturation with the vitamin is necessary in optimum health has little or no evidence in its support. In view of the fact that any fixed value in the plasma indicates a state of positive ascorbic acid economy, the saturation test has no place either as a diagnostic test for scurvy or as a criterion for the therapeutic administration of ascorbic acid. On the other hand, plasma-tolerance ascorbic acid curves may show promise as criteria for evaluating the previous intake and the extent of tissue stores.⁶⁴

Other Objective Tests

The Göthlin,⁶⁵ Dalldorf⁶⁶ and Rumpel-Leede⁶⁷ tests for capillary resistance are equivocal, positive or negative, in scorbutic and many nonscorbutic persons, and as a consequence should not be considered as precise diagnostic criteria. The intradermal test, in which the redox dye, 2,6-dichlorobenzenone indophenol, is injected into the skin and the time for the disappearance of color is used as an index of the status of ascorbic acid, has also been proved valueless.⁶⁸

TREATMENT OF SCURVY

The treatment of scurvy consists in placing the patient in a clean environment, if possible on bed rest, and the giving of approximately 1 gm. of ascorbic acid daily for about ten days. Synthetic vitamin C is recommended for obtaining a high dosage. If the synthetic preparation is unavailable, high vitamin C-containing foods — citrus fruits, tomatoes and certain berries — may be used. The parenteral administration of ascorbic acid is rarely indicated, but it may be done, if circumstances require this procedure, either intravenously or intramuscularly.⁶⁹ The presence of infections or other lesions concomitant with scurvy must not be neglected. The patient should receive a diet high in nutritional value to improve his general status;

some physicians administer high doses of the other vitamins as well as ascorbic acid in the treatment of scurvy. Anemia, when present, usually improves spontaneously or with iron. Following treatment, the patient should be instructed to continue on an adequate nutritional regime.

RELATION OF OTHER CONDITIONS TO ASCORBIC ACID ECONOMY

A sizable volume would be required to review all the diseases in which the therapeutic use of ascorbic acid has been attempted. Most of the empiricism for the use of this vitamin in diseases other than scurvy is derived either from the findings of low plasma values or from tissue unsaturation. It is now known that such methods of determining the ascorbic acid status are untenable, and there is consequently little evidence supporting the therapeutic use of ascorbic acid in conditions other than scurvy.

Dental and Gingival Disease

Since one of the most frequent changes that occur in scurvy is a swelling of the gums with bleeding, it has been reasoned that pyorrhea may be due to an inadequate intake of ascorbic acid.⁷⁰ Although it is true that in scurvy a superimposed infection may take place between the teeth and gums, pyorrhea usually exists independently of clinical scurvy.⁷¹ Low plasma ascorbic acid values in many patients with pyorrhea brought about the misleading conception that this disease is induced primarily because of a supposed prescorbutic condition. Pyorrhea is a disease of the gums due to an infectious process producing exudate, with the formation of pockets in the dentogingival space. The treatment of this condition is a local one and involves systemic care only when some other disease contributes to the process. Thus, the use of vitamin C in gingival lesions has a highly questionable foundation unless scurvy is present.

Diseases of the Gastrointestinal Tract

It has been noted by Warren, Pijoan and Emery⁷² that patients on Sippy diets (low in ascorbic acid) being treated for duodenal ulcers have low plasma ascorbic acid values. Portnoy and Wilkinson⁷³ found in their series of ulcer patients that the plasma ascorbic acid values ranged from 0.14 to 0.59 mg. per 100 cc. Others emphatically claim that ulcer patients have a deficiency of ascorbic acid.⁷⁴ Although it is admitted that the Sippy diet contains only about 5 mg. of ascorbic acid per day during the first week and about 15 mg. per day during the fourth week, the low plasma value found in a single determination does not mean either scurvy or a tendency to it. If a series of plasma or blood values tends to decrease — as contrasted with fixed low plasma levels — on the Sippy regime, it can be assumed that the dietary is insufficient in main-

taining a positive ascorbic acid economy and that this vitamin is being withdrawn from the tissues. Two cases have been reported in which scurvy developed, as might be expected, on an extended period of a Sippy diet.⁶⁰ There is no evidence that ascorbic acid affects the bleeding of ulcers in non-scorbutic subjects.⁶⁰

Rheumatic Fever

That ascorbic acid deficiency may be an etiologic factor in rheumatic fever was suggested by Rinehart,⁷⁵ whose general conclusion was that this disease is caused by the combined effects of ascorbic acid deficiency and infection. This point of view has been challenged by many.⁶⁰ The low plasma level of ascorbic acid so often found in patients with rheumatic fever indicates only the possible need for a greater ascorbic acid intake in the dietary to maintain a fixed plasma value. The fact that a low plasma value does not indicate scurvy at once limits the relation as expressed by Rinehart. Recently Kuttner⁷⁶ reported that the addition of vitamin C, as well as of other vitamins, did not reduce the incidence or recurrences of rheumatic manifestations in children with rheumatic fever. So far as can be determined, clinical scurvy has never been observed in acute rheumatic fever.

Tuberculosis and Other Infections

Although the patient with active pulmonary tuberculosis does not develop scurvy on an adequate intake of ascorbic acid, he requires, for some peculiar reason, more ascorbic acid in his dietary to maintain a high fixed plasma value of 0.7 mg. per 100 cc. than does a normal person.⁷⁷ Low levels are easily maintained by such patients on a so-called "average intake." This situation is true in many other infections. There is no evidence, however, that deficiency of this vitamin plays a specific role in the susceptibility to infections in human subjects.

Wound Healing

Since it has been emphasized by Wolbach and Howe³³ that the fundamental lesion in scurvy is due to a lack of intercellular substance and poor capillary formation, interest was soon directed to the study of experimentally produced wounds in latently and frankly scorbutic guinea pigs.⁷⁸ Wounds of scorbutic guinea pigs healed slowly and with poor tensile strength. In fact, a relation has been established between the wound ascorbate value and its tensile strength in scorbutic and prescorbutic guinea pigs.⁷⁹ On the other hand, with the exception of Crandon's work,³ studies of wound healing in human subjects have not been sufficiently controlled. So far, the evidence that ascorbic acid is necessary for wound healing in the nonscorbutic subject has no foundation whatsoever. Crandon³ after three months of an ascorbic acid-free diet, with no plasma ascorbic acid for several months,

had perfectly normal wound healing as revealed by biopsies. It was only after he had developed clinical scurvy that wound healing was impaired. Since other reports in the literature indicate that low values of ascorbic acid may influence wound healing,⁸⁰ and since in such studies there were no human subjects as basic controls, one of us (M. P.⁸¹) made observations on a man who remained on a low vitamin C intake for twenty months. No foods containing significant quantities of ascorbic acid were consumed. A few well-cooked vegetables, whose acid content was negligible as determined by assays, were eaten from time to time. The dietary was as low in ascorbic acid as could be comfortably endured. The average intake averaged 16 mg. a day for twenty months, and at no time was it more than 25 mg. or less than 12 mg. The plasma ascorbic acid value remained for the most part at zero with occasional high increases, never exceeding 0.2 mg. The white cell-platelet layers, on the other hand, always exceeded 25 mg. per 100 gm. At the end of this period, while the patient was on the same diet, a wound was made in the left mid-back consisting of an incision 2.5 cm. in length and 1 cm. in depth into the subcutaneous tissue. Ten days afterward a biopsy revealed normal healing with ample intercellular substance and capillary formation.

It is thus evident that a daily dietary intake of ascorbic acid of between 12 and 25 mg. that maintained an extremely low plasma level but a value of 25 mg. or more per 100 gm. in the white cell-platelet layer was sufficient to produce adequate wound healing and collagen formation.

DIETARY FACTORS

Since it is our thesis that the amount of ascorbic acid required by the human subject is that sufficient to maintain an adequate tissue level, thus preventing scurvy, it is of interest to discuss briefly certain considerations relating to the foods that are rich in vitamin C.

Many reports have already appeared in the literature that deal with the ascorbic acid content of foods. Losses of the vitamin through processing have been studied by King and his associates.⁸²⁻⁸⁴ Their studies indicate that the loss of ascorbic acid is due to two essential factors: oxidation of ascorbic acid and the transfer of the vitamin to cooking fluids. Their assays and those of others stress the point that cooking may cause a considerable loss of the vitamin. Aside from this, there is a remarkable variation in the ascorbic acid content of a specific food. This may be due to a seasonal variation and to methods of storage. For instance, summer-grown tomatoes may contain as high as 25 mg. per 100 gm.,⁸⁵ whereas those purchased in April may average only 4 mg. per 100 gm.⁸⁶ Such variations are found to a greater or lesser degree in the majority of fruits and vegetables. Lately,

Pijoan and McCay⁸⁷ have collected sufficient data to show that values of ascorbic acid as expressed in standard food tables may be in error to the extent of 75 per cent and that the various methods of food preparation modify the content of ascorbic acid. There are many ways of minimizing the losses of this vitamin.⁸² There is, furthermore, the question of dehydroascorbic acid in foods. Chemically derived dehydroascorbic acid has been shown to be antiscorbutic, but it is somewhat questionable whether the dehydroascorbic acid in food is antiscorbutic. Nevertheless, one should assume for the present that until proved otherwise dehydroascorbic acid — no matter where found — protects against scurvy.

Because the cooking and processing of food effect a variable but at times considerable reduction in its antiscorbutic property, it is indeed fortunate that the daily requirements are not great.

* * *

The use of ascorbic acid, either synthetic or in the diet, is for the prevention or treatment of scurvy. With the possible exception of its influence on amino acid metabolism in premature infants, no other role can be ascribed to the vitamin.

A diet cannot be condemned as deficient in this vitamin unless a continued linear decline of the content of the vitamin in the whole blood, white cell-platelet layer or other tissue takes place, the appearance of scurvy being conclusive evidence.

Relatively small amounts of the vitamin — possibly 25 mg. or under a day — are necessary to maintain fixed blood or white cell-platelet levels. Any fixed level of the vitamin in the plasma, irrespective of how little is present, indicates a nonscorbutic process and a positive body economy.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30271

PRESENTATION OF CASE

A sixty-nine-year-old man was admitted to the hospital because of old draining sinuses of the back.

The patient had been in apparent good health until about one and a half years before entry, when he complained of pain in the back, which was diagnosed as right sacroiliac strain, and treated by brace and strapping. He continued to have pain in the back. About one year prior to admission he fell on the ice and shortly thereafter a slight swelling appeared in the midlumbar region. A few months later this suddenly ruptured, liberating a large quantity of clear fluid. This continued for three weeks, after which the character of draining material changed to pus, with considerable cheesy material intermingled with it. He entered a community hospital, where the draining area was incised and x-ray films were taken. His condition progressively became worse, however, and he was sent to this hospital. Some time during the year preceding hospital entry, he had noted a swelling in the right groin. No other information was available.

Physical examination showed a well-developed, somewhat cachectic man in no distress. He was quite confused. The heart was slightly enlarged. The lungs were clear. A large ovoid, nontender, elastic, nonfluctuant, noninflamed swelling was present in the right groin. In the lumbar region on the back there were three draining sinuses, from which mucopurulent material exuded. The entire skin of the spine was loose. No true points of tenderness were found.

The blood pressure was 166 systolic, 100 diastolic. The temperature was 101°F., the pulse 92, and the respirations 15.

Examination of the blood showed a white-cell count of 27,400, with 92 per cent neutrophils. The hemoglobin was 8.2 gm. per 100 cc. A Hinton test was negative. The urine was acid, with a specific gravity of 1.020 and a ++ test for albumin. The blood nonprotein nitrogen was 35 mg., and the protein 5.9 gm. per 100 cc.; the chloride was 97.6 milliequiv. per liter.

X-ray examination of the lumbosacral spine showed mottling, loss of bony detail and areas of

increased density and irregularity of both the upper and lower surfaces of the fifth lumbar vertebra. The right lumbosacral joint was also indistinct. The left sacroiliac joint was normal.

A culture of the pus from the sinuses gave a coagulase-positive, hemolytic *Staphylococcus aureus* and diphtheroids. Three smears showed gram-positive cocci in clumps. No acid-fast organisms were seen.

The patient was given several transfusions and intravenous fluids. On the third hospital day incision and drainage of the abscess in the right groin was carried out, with removal of 1000 cc. of thick greenish pus. The abscess seemed to extend retroperitoneally, but a lipiodol injection showed no connection with the draining sinuses in the back, with the fifth lumbar vertebra or with the right hip joint, although the dye passed down for a distance of 8 cm. on the anterior aspect of the leg. A culture of the abscess yielded a hemolytic *Staph. aureus* and diphtheroids. Cultures for fungi were negative.

The patient's condition improved slightly. The temperature ranged between 98.6 and 102°F. On the eighth hospital day he was given 3 gm. of sulfadiazine. For the next five days the temperature was below 101°F. On the thirteenth hospital day he had a sudden rise of temperature to 103°F., which fell after a few hours to 100°, with subsequent spiking to 103° for the next two days, when it again fell to about 100°. On the seventeenth hospital day an abscess in the left buttock was drained, giving 300 cc. of the same type of purulent material. Smears and cultures of the material again yielded a hemolytic *Staph. aureus* and diphtheroids. A blood culture was negative. Beginning on the eighteenth hospital day, he was daily given penicillin intramuscularly every four hours (a daily total of 135,000 units) and 2500 units locally for six days. The character of draining material became mucoid and decreased somewhat, and the temperature came down to normal. On the twenty-fourth hospital day, examination showed occasional rales in both lungs. The liver was enlarged and tender. X-ray films of the chest showed no gross consolidation; there were mottled areas of increased density in both upper lung fields, and a small area lateral to the right hilus.

He continued to receive transfusions and intravenous fluids. On the twenty-seventh hospital day, a 300-cc. hematoma was found in the right groin; this was removed, and the bleeding point, which appeared to be an artery, was ligated. The temperature again spiked to 102 and 103°F. On the twenty-ninth hospital day a left ischiorectal abscess was incised and drained, giving purulent fluid. On that day he was again placed on a similar dosage of penicillin for six days; it was then omitted for three days and resumed for another eight days. From the twenty-eighth until the fifty-fifth hospital day

*On leave of absence.

the temperature remained normal. Re-examination of the lumbar spine on the forty-fifth hospital day showed an increase in the area of destruction of the anterior lower surface of the fifth lumbar vertebra. Little change was seen in the anterosuperior margin of the sacrum. Because of the destruction of the fifth lumbar vertebra, the interspace was considerably widened anteriorly. No soft-tissue shadow was visible in this region either in the anteroposterior or the lateral view. The hip joints showed no change. During the period in which the temperature was normal and drainage decreased he continued to lose weight and no evidence of healing could be seen. On the fifty-fifth hospital day he suddenly had a chill and a rise of temperature to 104°F., and of pulse to 140.

Physical examination was the same as before. A urine examination showed many white cells. A urine culture gave abundant growth of colon and proteus bacilli and gram-positive cocci in chains were seen in a stained smear. A blood culture was negative. Culture of the draining sinuses in the back still yielded a hemolytic *Staph. aureus* and diphtheroids, as well as *Clostridium welchii* and a species of *Alcaligenes*. Culture of the groin gave a hemolytic staphylococcus and diphtheroids. The white-cell count was 14,200, with a hemoglobin of 11.8 gm. per 100 cc.

The patient was given intravenous fluids, blood transfusions and 4 gm. of sulfadiazine. He continued to receive sulfadiazine daily for the next twenty-eight days, the blood sulfadiazine level reaching 5.2 mg. per 100 cc. During that time the urine continued to show many white cells and gave a ++ or +++ test for albumin; the temperature spiked to 103°F. on one or two occasions, but most of the time the temperature was about 101°. Although drainage from the various sinuses decreased, no evidence of healing could be seen, and the patient failed to gain weight.

On the seventy-third hospital day, his face became puffy. This increased during the next two weeks. X-ray re-examination of the spine on the seventy-eighth hospital day showed no definite change in the appearance of the fifth lumbar vertebra and of the adjacent surface of the sacrum; there was possibly a little new bone formation about the anterior margin of the first sacral segment. The fourth lumbar interspace appeared to be a little narrowed, and the right lower margin of the fourth lumbar vertebra showed a small area of irregularity suggesting destruction. Sulfadiazine was stopped on the eighty-third hospital day, and he was given bladder irrigations without any change in the character of the urine. From the eighty-seventh to the ninety-first hospital day the temperature gradually rose from 100 to 104°F. On the eighty-ninth hospital day he developed nausea and vomited several times. The nonprotein nitrogen was 84 mg. per 100 cc.; the serum protein was 5.1 gm. per 100 cc., and

the urine was the same as before. A plain film of the abdomen showed considerable gas distributed through many loops of the small intestine, none of which appeared to be abnormally dilated. There was gas in the stomach, but little in the colon.

On the ninety-fourth hospital day he developed jaundice and became comatose. The serum bilirubin was 7.6 mg. per 100 cc. direct, and 9.5 mg. indirect. The jaundice increased, the nonprotein nitrogen rose to 96.5 mg. per 100 cc., and the patient died on the ninety-sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT N. NYE*: I am not sure what is the best way to discuss this case, but I am going to say that I believe this man had tuberculosis of the spine, in spite of the fact that he was sixty-nine years old, and discuss the high points in the course of his disease on that basis. Of course in any man of this age with pain in the back the first thing one should think of is neoplasm of some sort, particularly metastatic cancer. But from the course of the disease, I do not believe that cancer is probable.

The man had been sick for approximately one and a half years before he entered the hospital. Of course the onset noted in the history was following a fall on the ice; but I doubt if that had anything to do with the actual disease itself. The record says that after this fall he had a slight swelling in the mid-lumbar region and that a few months later this suddenly ruptured, liberating large amounts of clear fluid. That is difficult to explain, but one might question whether it was an accurate observation. Certainly if it was tuberculosis of the lumbar spine and there was abscess formation that had dissected out to the back, one would not expect the fluid to have been clear. On the other hand, the chances are that it would not have been frank pus. Possibly because of the fact that it was not frank pus, the note is made that the fluid was clear. I also doubt the large quantity, because I should not expect appreciable amounts to be extruded in this condition.

The discharge then became purulent; in other words, it was secondarily infected. The record says that there was considerable cheesy material intermingled with the pus and that some time during the period prior to admission the patient noticed swelling in the right groin. It is not unusual for a tuberculous abscess of the spine to dissect in various parts of the body, and in this man the abscess in the groin was probably due to dissection following the psoas muscle, which is one of the favorite places for dissection from the lower part of the spine.

When the patient entered the hospital he had apparently lost considerable weight; he had fever, an elevated pulse and normal respirations. As one

*Assistant pathologist, Boston City Hospital; assistant professor of bacteriology, Harvard Medical School.

would expect, the white-cell count was elevated, with a high percentage of neutrophils. The hemoglobin was quite low, but one must realize that the disease had been going on for some time and that the man had probably not received ideal care. It is interesting that he showed a ++ test for albumin on admission. Whether that means that the man had a benign nephrosclerosis or that the inflammatory process had gone on to produce changes in the kidneys is questionable. The nonprotein nitrogen of course was high normal. X-ray examination of the lumbosacral spine showed a destructive lesion. Is there anyone here to demonstrate the films?

DR. MILFORD SCHULZ: Here we see the destructive lesion involving the body of the last lumbar segment. The faces of the adjoining vertebra are surprisingly intact. This is curious for a tuberculous process, although that does not necessarily rule it out. The superior surface of the sacrum looks a little bit irregular, and on later examination the inferior aspect of the fourth segment is involved. I do not believe that we can help you much.

DR. NYE: Have you the x-ray films of the chest?

DR. SCHULZ: Yes, but there is nothing that is incriminating. The findings described must have been found on another examination of the chest.

DR. NYE: In other words you question whether there was evidence of a pulmonary lesion. Of course that might have been based on a fluoroscopic interpretation.

DR. SCHULZ: Either that or other films of the chest were available.

DR. NYE: The x-ray films of the chest are of little assistance. Of course there was a destructive process in the fourth and fifth lumbar vertebrae that also involved the sacrum, and we shall have to let it go at that.

Culture of pus from the sinuses yielded a coagulase-positive hemolytic *Staphylococcus aureus*. That, I believe, was a contaminant. Of course a coagulase-positive hemolytic *Staph. aureus* is usually a virulent organism, but at the same time it does not have to be the primary etiologic agent. It can be a secondary invader of sinuses due to tuberculosis or to some other type of chronic draining infection.

Three smears showed gram-positive cocci in clumps. In other words they were probably looking for one of the unusual organisms, such as an Actinomycetes, which I shall mention in the differential diagnosis; but it appears that no so-called "sulfur granules" or gram-positive filaments that might suggest the organism of actinomycosis were observed. Also, no acid-fast organisms were seen, which one would not necessarily expect in direct smears even if this were tuberculosis.

The abscess in the groin was drained, and one liter of thick, greenish pus was obtained. This cavity, when it was injected, showed no connection with the process in the vertebra, but that does not necessarily mean that it did not rise there. Culture of

that pus yielded the same organisms — staphylococcus and diphtheroids — as the culture from the draining sinuses, which is reasonably good evidence that they were the result of one and the same process. It also says that cultures for fungi were negative. In other words, they probably tried to isolate one of the blastomycotic organisms. These yeastlike fungi grow reasonably well on ordinary culture mediums, and the fact that they were not obtained is fair evidence that this was not the etiologic agent.

The patient then developed an abscess in the buttock, which was probably due to dissection from the same process. This also yielded a staphylococcus and diphtheroids. At about the same time, around the twenty-fourth hospital day, the liver was large and tender. One thing that I have learned in looking over two of these cases every week is that a large liver clinically does not necessarily mean a large liver pathologically. I am doubtful of the significance of this large liver, but there are signs of liver disease later, and this may have some significance, possibly an extension of the process to the liver. I cannot explain the tenderness.

The next point, of course, is that the x-ray film of the chest showed mottled areas of increased density, but as you have seen, the film appears to be essentially negative. A hematoma developed in the groin abscess, which has little significance since this was a destructive lesion and undoubtedly an artery was involved.

Under penicillin, the temperature came down to normal and stayed normal for two or three weeks. Probably some of the fever was due to the absorption of products from the secondary infection, which was massive, and the penicillin may well have controlled that. But in spite of the drop in temperature, he continued to lose weight, and there was no evidence of healing of the sinuses. At about that time the kidneys began to show signs of involvement. The patient had a chill. The urine sediment contained many white cells, and a culture showed colon and proteus bacilli; gram-positive organisms in chains were seen in a smear, but individual colonies could not be obtained because of the spreading colonies of the proteus bacillus. The fact that the organisms were different from the organisms recovered from the various abscesses suggests that this was not due to a pyemic infection of the kidney — something coming from the blood stream or possibly by direct extension from the abscess that was already present — but rather to an ascending infection caused by the colon bacillus, which probably indicates a developing pyelonephritis. Again, the blood culture was negative, and the cultures from the sinus in the back still yielded a staphylococcus and diphtheroids as well as the Welch bacillus and a species of *Alcaligenes*, neither of which is important. The Welch bacillus is a habitant of the normal stool and is apt to be found in secondarily infected wounds like this; in the absence of

symptoms of gas-bacillus infection it has no significance.

Two days before death the patient developed jaundice and became comatose; the bilirubin was 7.6 mg. direct, and 9.5 mg. indirect. I do not know what the significance of that is. In cases of sepsis one frequently gets so-called "septic jaundice." Kimmelstiel* has mentioned cases of this sort which at autopsy showed little if anything specific in the liver and in which the jaundice was probably due to some terminal toxic condition. I do not know whether this amount could be accounted for on that basis. Do you, Dr. Richardson?

DR. WYMAN RICHARDSON: I do not believe so. Most of it was determined by the direct method.

DR. NYE: If this is not tuberculosis, what other diseases should one consider in which there are draining sinuses that refuse to heal?

One should always think of actinomycosis, probably an actinomycotic lesion in the spine. It does occur, but is usually secondary to some other process elsewhere, either to pelvic actinomycosis or to peritoneal or abdominal infection following a ruptured appendix. Furthermore, it is said that the actinomycotic lesion of bone is usually around the bone rather than in the bone, and I take it that this destructive process involved the body of the vertebra. Another thing is that no sulfur granules were found and that a smear showed only gram-positive cocci.

Another possibility is a chronic blastomycotic infection. These are extremely rare, and I have never heard of one involving the spine. Again the organism should have been cultured from the pus.

Another possibility is a chronic osteomyelitis due to a pyogenic organism. The commonest ones are staphylococcus and streptococcus, and occasionally pneumococcus, the typhoid bacillus and certain other of the gram-negative enteric bacilli. The history, however, does not sound like what one would expect with a chronic pyogenic osteomyelitis. Furthermore, I believe that in cases of chronic osteomyelitis there is usually evidence in the x-ray films of new-bone formation, such as in a Brodie abscess, which was not present in this case.

Tertiary syphilis or gumma of the bone might occur. It certainly would be extremely unusual for it to have a course such as this. Also, a Hinton test was negative, although we have recently had two cases of gumma at the Boston City Hospital in which the Hinton test was negative.

This man probably had amyloid disease. He had had a chronic infection on the basis of tuberculosis with secondary infection over a period of at least a year, possibly longer. This might well have accounted for the development of pyelonephritis in the kidney, which is a frequent sequela of amyloid disease in the kidney. It may also have accounted

for the evidence of liver failure at the end, although again I cannot rule out entirely some infectious process.

I believe that this patient had tuberculosis of the spine, with abscess formation, secondary pyogenic infection and dissection and pyelonephritis, probably on the basis of amyloid disease of the kidneys; the liver at autopsy probably showed little if anything, except for the possibility of amyloid disease.

DR. RICHARDSON: I am guessing this patient had actinomycosis: first because it seems to me that he had an excessive amount of pus, second because we rarely find actinomycosis here in this hospital when we look for it, and third because we have been told that there have been three cases of actinomycosis here recently, two of which have been discussed at these conferences, and since these rare things always go in threes, perhaps this is the third case.

DR. EARLE M. CHAPMAN: I saw this patient only once. I shall read briefly from my note in the record at that time:

The long duration of his illness and the failure to respond to penicillin and, I presume, to sulfonamide therapy, suggest that this process is either tuberculous or saprophytic, and also that the patient has failed to develop antibody to the causative organism. . . . The outlook seems grim. I have little to offer, although it would be well to do a skin tuberculin test, a flat film of the abdomen for question of abscess about the liver, an x-ray film of the chest and a culture for typhoid organisms.

DR. FLETCHER H. COLBY: I saw this patient a good many times toward the end of his illness. At that time his face was very puffy, but he had been given large amounts of testosterone and I understood that the puffiness of the face could be attributed to that. He did not have generalized edema. I saw him simply because he was a terrific nursing problem. He had had no previous urinary symptoms, but at some period earlier he had developed an urgency of urination that amounted to incontinence, and could not avoid wetting the bedclothes, so he was put on constant drainage. His urine was always purulent. He had many reasons for having purulent urine — constant drainage and infection by the proteus bacillus and other organisms. It seemed quite probable that he had a severe cystitis or possibly a pericystitis, with some possibility, which we never investigated, of actual fistula between the bladder and the abscess in the pelvis. This has occurred in patients with chronic osteomyelitis.

CLINICAL DIAGNOSES

Osteomyelitis, fifth lumbar vertebra (*Staph. aureus*).

Toxic hepatitis.

DR. NYE'S DIAGNOSES

Tuberculosis of spine, with abscess formation, secondary infection and dissection.

*Kimmelstiel, P. Symptom of jaundice occurring in newborn differential diagnosis. *Bull. Charlevoix Mem. Hosp.* 15:20, 1944

Pyelonephritis (probably secondary to amyloid disease of the kidneys).

Amyloid disease of liver?

ANATOMICAL DIAGNOSES

Tuberculosis of lumbar vertebrae, with paravertebral, psoas, groin and perinephric abscesses.

Tuberculosis of spleen, liver, left adrenal gland and bronchial lymph nodes.

Acute hepatitis, severe.

Jaundice.

Cystitis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy showed that the fourth and fifth lumbar vertebrae were involved in a necrotic process. There was a large

the spleen and liver contained several tubercles. The jaundice, however, was due not to a diffuse tuberculosis of the liver, but to a very acute necrotizing hepatitis, with widespread central destruction of the liver cells involving about two thirds of the parenchyma (Fig. 1). The liver cells were completely wiped out in many places, and there was a marked polymorphonuclear infiltration. The liver cells that were still recognizable as such were swollen and granular. There was no evidence of amyloid disease anywhere.

With the amount of liver destruction that this patient had it is difficult to explain the absence of clinical signs of liver damage until two days before death. Undoubtedly the liver damage was the immediate cause of death, and I believe that it

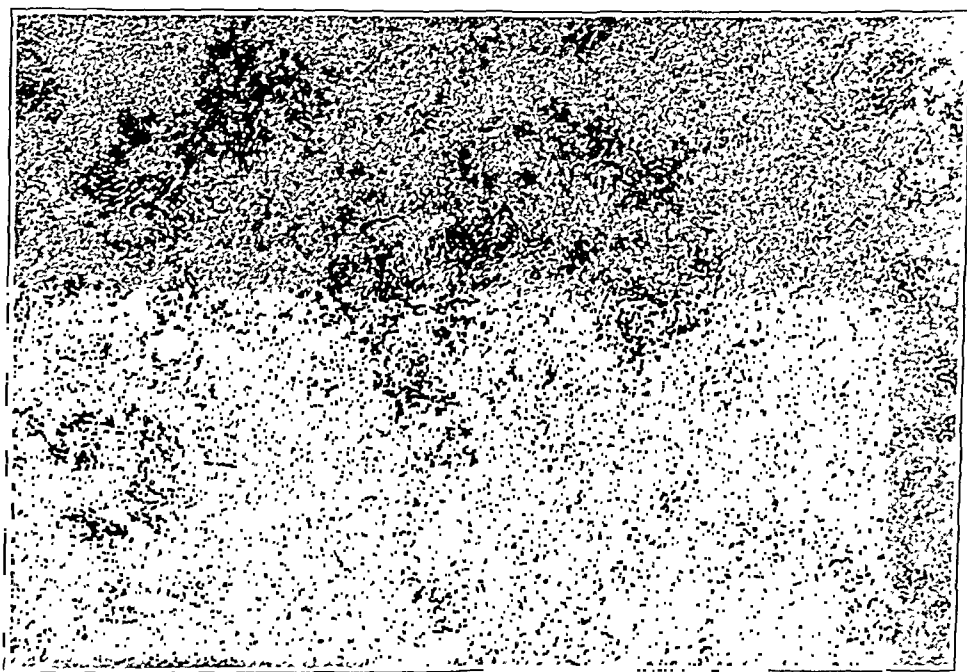


FIGURE 1.

abscess that involved the psoas muscles and communicated with a large perinephric abscess on the left side, which was filled with purulent material. He also had, of course, the draining sinuses and the abscess in the groin.

DR. COLBY: Did he have cortical abscesses of the kidneys?

DR. CASTLEMAN: No; the kidneys themselves were free from infection.

The bladder was injected and slightly trabeculated. The prostate was slightly enlarged. The liver was normal in size, slightly greenish and moderately soft. The adrenal glands were caseous, which at the time of autopsy gave a clue to the correct diagnosis. The microscopic sections showed tuberculosis of the vertebrae and of the adrenal glands, and

was directly related to the secondary infection.

Dr. Nye, how common is it to find a secondary invader so fulminating as this associated with tuberculosis?

DR. NYE: The patient never had a bacteremia during life. What were the findings at autopsy?

DR. CASTLEMAN: We were unable to recover a staphylococcus from the blood stream.

DR. NYE: I do not know how to explain the liver lesions. It is true that most chronic tuberculous infections that drain become secondarily infected. I should say that the severity of the secondary infection is dependent on the type of organism. Streptococcal infections are sometimes followed by extensive and even fatal hepatitis of the acute-yellow-atrophy type. A coagulase-positive *Staphylococcus*

aureus is a reasonably virulent organism under most circumstances, and that may have been the explanation.

CASE 30272

PRESENTATION OF CASE

A thirty-eight-year-old housewife was admitted to the hospital in coma.

The history was quite unsatisfactory and incomplete. She was first seen by her physician about three weeks before admission, at which time she gave a history of rheumatic fever in youth, with the recent development of increasing dyspnea, orthopnea and ankle edema but without fever or chest pain. Examination showed an enlarged liver, extending two or three fingerbreadths below the costal margin. Both lung bases were filled with rales. The heart was fibrillating, and apical systolic and diastolic murmurs were heard. She was placed on a salt-free diet, with limited fluid intake, 0.1 gm. ($1\frac{1}{2}$ gr.) of digitalis and 3 gm. of ammonium chloride daily and Mercupurin every three days. The pulse fell from 110 to 75, without change in the blood pressure, which was about 145 systolic, 90 diastolic. On this regime she improved rapidly, the ankle edema disappeared and she resumed her daily activities.

Two days before entry, while standing, she suddenly began to talk strangely, cried and felt depressed. Then without any convulsion or other complaint she fell to the floor in coma. She became aphasic, incontinent of urine and feces and unable to take anything by mouth. She could apparently move only the left side of the body.

Physical examination showed a well-developed, well-nourished comatose woman, with dry skin covered by many psoriatic lesions. The left pupil was smaller than the right. The pupils reacted to light, but the eyes wandered aimlessly. The fundi were normal. The lungs were clear. The left border of cardiac dullness was 13 cm. to the left of the midline in the fifth space. The sounds were distant. The heart was fibrillating. There was an apical systolic murmur. The aortic second sound was weaker than the pulmonic. The abdomen was negative except for the liver, which extended two fingerbreadths below the costal margin. The right arm and leg were paralyzed, with slightly hyperactive reflexes and bilateral positive Babinski signs. The neck was slightly stiff.

The blood pressure was 250 systolic, 120 diastolic. The temperature was 102.5°F., the pulse 100, and the respirations 25.

Examination of the blood showed a white-cell count of 12,800. The urine gave a specific gravity of 1.020 and a +++ test for albumin. The blood nonprotein nitrogen was 84 mg. per 100 cc., and the protein 7.2 gm. Blood Hinton and Wassermann

tests were negative. A lumbar puncture showed little if any increase in pressure. The fluid was clear and contained 80 lymphocytes and 20 polymorphonuclears per cubic millimeter; the total protein was 51 mg. per 100 cc., and the gold-sol curve 0023321000.

A stomach tube was passed, through which she was fed. She was given 0.1 gm. ($1\frac{1}{2}$ gr.) of digitalis and 1 gm. of ammonium chloride daily. She was quite restless and required restraint and paraldehyde almost every day.

On the second hospital day she developed Cheyne-Stokes respirations. The temperature, which had been steadily rising, went to 106°F. Coarse rales were heard in both bases, with many squeaking rales in the upper lung fields. She died on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. AUGUSTUS S. ROSE: This case raises the perennial differential diagnostic problem — cerebral hemorrhage, thrombosis or embolism. When the record is first read the diagnosis seems clear; a second reading, however, makes another diagnosis seem just as evident; and a third reading, I confess, dispels one's conviction of either diagnosis.

The difficulties of clinical differentiation of apoplexy are notorious. Last evening I read the description in four modern textbooks of neurology and one of general medicine and found agreement only in that the diagnosis is difficult. Current literature offers little help. An article by Aring and Merritt* on the clinical differentiation between cerebral thrombosis and cerebral hemorrhage is excellent, but gives little aid in the immediate problem because of the strong implication of embolism.

This thirty-eight-year-old woman was apparently well until she developed clear-cut evidence of congestive heart failure in association with rheumatic heart disease. Appropriate medical therapy brought prompt improvement, but on return to activity she suddenly talked queerly, indicating involvement of the speech mechanism, and immediately fell to the floor in coma, with a right hemiplegia. When examined at the hospital two days later she was found to have a restless coma, a right hemiplegia, bilateral positive Babinski signs and unequal pupils.

The heart was fibrillating, and there were signs of congestive failure.

The spinal fluid was clear and colorless, containing 100 white cells per cubic millimeter but no red cells. The spinal-fluid pressure was within normal limits.

This spinal-fluid picture is certainly a surprise, and difficult, if not impossible, for me to fit with

*Aring, C. D., and Merritt, H. H. Differential diagnosis between cerebral hemorrhage and cerebral thrombosis: clinical and pathological study of 245 cases. *Arch. Int. Med.* 56:435-456, 1935.

the clinical picture. With cerebral hemorrhage, increased pressure and red cells are to be expected. With embolism and thrombosis, normal pressure and slightly yellow fluid with both white and red cells are usual.

The characteristic clinical picture of cerebral thrombosis differs considerably from what we have in this case. It is found in middle-aged or elderly patients with evidence of long-standing vascular disease. Signs develop slowly or at rest. Deep coma occurs if a sufficiently large vessel is involved, but most frequently it is a quiet, not a restless, coma. Pupillary difference is not usual, and many patients recover from the first episode, or at least live for many days.

Exclusion of hemorrhage or embolism is more difficult.

If for the moment we disregard the cardiac history and physical findings, we have a clinical picture that fits reasonably well with that seen in massive intracerebral hemorrhage, with the exception of the spinal fluid. Restlessness, coma, stiff neck, unequal pupils and bilateral Babinski signs can be evidence of midbrain compression, which is not infrequent in intracerebral bleeding. There is, however, no suggestion of pre-existing hypertension, and we cannot ignore the cardiac situation.

This patient had the ideal set-up for the development of a cerebral embolus. She had rheumatic heart disease, with auricular fibrillation and probable mitral stenosis. Having had a period of congestive failure and the accompanying cardiac dilatation, she had, on returning to activity, the rapid but not instantaneous onset of coma. By all logic, therefore, she must have had embolism. The neurologic manifestations should, however, be considered more closely.

The first symptom of queer, confused talk clearly points to interruption of the blood supply to the dominant hemisphere, but the rapidly ensuing coma suggests more widespread involvement than the branches of the left middle cerebral artery. Possibly the entire middle cerebral artery was occluded. But death followed more quickly than one would expect from occlusion of this artery alone. Furthermore, the signs suggesting midbrain compression do not fit. It is therefore necessary to suppose multiple lesions or to find the single lesion that would explain the brain-stem signs as well as the first symptom of confused speech. Occlusion of the vessels of the medulla would not produce this total picture, and although occlusion of the basilar artery could produce the neurologic signs, I do not believe that its occlusion would give the onset as seen in this case.

I am therefore left with the probable diagnosis of multiple cerebral embolism. The spinal-fluid cell count of 100 white cells, with 20 per cent polymorphonuclears, taken alone points to an infectious process, but we have no other evidence of infection.

DR. WYMAN RICHARDSON: How do you explain the renal findings?

DR. ROSE: I thought that they were of no particular importance regarding the cerebral affair or as a contributing cause of her death. The specific gravity of 1.020 suggests a reasonably good function, although if the dry skin, the albumin and the elevated blood nonprotein nitrogen are considered to be evidence of dehydration, the specific gravity should have been higher. I cannot see how these findings would have contributed to the cerebral episode unless they are evidence of a pre-existing vascular nephritis and a hypertension.

DR. RICHARDSON: You could, if you wanted to go rather far afield, say that she had a silent bacterial endocarditis associated with embolic nephritis. Of course that association is not infrequent. If one assumes that she had small emboli in the meninges from bacterial endocarditis, what sort of spinal fluid would have been found?

DR. ROSE: It would have been slightly hazy with not only white cells but also red cells, and probably some xanthochromia. In cerebral hemorrhage, too, one would expect xanthochromia, or even with thrombosis when the fluid is obtained as early in the course of the illness as this. I should call the absence of red cells in the spinal fluid the best indication that there were no infected emboli. In other words, the fluid was more inconsistent with emboli from bacterial endocarditis than with cerebral hemorrhage or embolism.

DR. JAMES B. AYER: Dr. Rose has referred to Aring and Merritt's paper; I should like to ask him what they say about the fluid in cases with a septic embolus.

DR. ROSE: Red cells are almost always present.

DR. AYER: Two years ago I saw a case of bacterial endocarditis in which emboli were being thrown off from time to time; the spinal fluid was slightly cloudy but contained no red cells. I believe that I have seen one other case without enough red cells to color the fluid.

DR. BENJAMIN CASTLEMAN: Does it not depend, Dr. Ayer, on the fact that if the emboli go to the meninges there results what may be called a bacterial meningitis, with red cells in the spinal fluid, whereas if they go to the large vessels within the brain, they produce infarction that does not necessarily come to the surface or reach the ventricular system?

DR. AYER: Or on whether there is subsequent hemorrhage into the area.

CLINICAL DIAGNOSES

Cerebrovascular accident.
Hypertensive, rheumatic heart disease.
Auricular fibrillation.
Psoriasis.

DR. ROSE'S DIAGNOSES

Rheumatic heart disease, with mitral stenosis.
Cerebral embolism, multiple.

ANATOMICAL DIAGNOSES

Rheumatic heart disease, with mitral, aortic and tricuspid stenosis.
Subacute bacterial endocarditis: mitral valve and left auricle.
Cerebral embolus: left internal carotid and middle cerebral arteries.
Cerebral infarction.
Embolic nephritis.
Pulmonary infarcts.
Thrombosis: posterior tibial vein.
Myocardial infarcts, miliary.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy, Dr. Charles S. Kubik found an embolus involving the terminal portion of the left internal carotid and the proximal portion of the middle cerebral artery that had produced infarction of the entire area supplied by the left middle cerebral artery and also a large part of the frontal lobe anteriorly, which is supplied by the anterior cerebral artery. The softening included the lenticular nucleus, the caudate nucleus and the internal capsule; in several small regions the soft tissues were hemorrhagic. Although he could not rule out

a localized thrombosis, he leaned a bit more toward embolism.

The autopsy also showed an enlarged heart, weighing over 600 gm., with rheumatic stenosis of the mitral, aortic and tricuspid valves, and a superimposed bacterial endocarditis of the mitral valve. There was an extensive bacterial endocarditis of the left auricle above the mitral valve, with the formation of mural thrombi, one of which, I believe, migrated to the internal carotid artery and produced the infarction.

The renal disease was embolic nephritis from the subacute bacterial endocarditis.

DR. ROSE: There were no red cells in the urine?

DR. CASTLEMAN: None are recorded.

This patient also had something unsuspected. There were numerous pulmonary infarcts that had been produced by emboli from thrombi in one of the posterior tibial veins. There was no jaundice.

DR. RICHARDSON: I believe that this is a characteristic feature in so-called "embolic nephritis" — a reasonably normal specific gravity and large amounts of albumin, although I should expect that there would also have been red cells. The last frequently appear in showers and might be missed in one examination.

DR. CASTLEMAN: There were small emboli to the heart itself, with miliary infarcts in the myocardium.

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(d) *Maternity benefits.* Any female employee shall be entitled to cash sickness benefits for a period of six weeks of disability because of pregnancy provided such employee has been under this act for a period of not less than ten months. Hospital benefits for such female employee shall not exceed a rate of \$4 per day for a period up to ten days and such employee shall be allowed for delivery expenses the sum of \$50. Such employee may choose a physician of her own choice provided such physician is duly licensed in this commonwealth.

SECTION 5. *Coverage.* In order to promote the health, safety and welfare of employees, every employer under this act shall provide a voluntary system for the payment of benefits to his employees who are under this act in the following manner:

(a) *Insurance.* By procuring an insurance policy from an insurance company authorized to do business in this commonwealth in such form as may be required by the Insurance Commissioner. The employer shall be entitled to reimbursement for one half the cost of such insurance from his employees by payroll deductions. Such policy shall not be effective until the premium charges shall be approved by the Insurance Commissioner as adequate, fair and reasonable; or

(b) *Self-insurance.* By furnishing the Industrial Accident Board satisfactory proof of his financial ability to pay the benefits prescribed by this act to his employees by furnishing securities, bond or indemnity in an amount satis-

factory to the Industrial Accident Board; such employer shall be entitled to reimbursement from his employees for one half the cost of the coverage by payroll deduction. The premium charges for such indemnity or bond or any other form of insurance contract shall be approved by the Insurance Department as adequate, fair and reasonable. The forms for such indemnity, bond or other insurance contract shall be approved by the Insurance Commissioner.

(c) *Rules.* The Industrial Accident Board may make rules consistent with this act for the proper carrying out of its provisions.

SECTION 6. *Termination.* An employee's right to benefits under the provisions of this act terminates on the date he severs his employment unless on that date he is suffering a disability which entitles him to the benefits provided herein. An employee may terminate his rights to the benefits under this act by giving to his employer a notice in writing effective upon the expiration of thirty days.

SECTION 7. *Hearings and appeals.* Any employee, self-insured employer or insurance company may request the Industrial Accident Board for a hearing at any time on the issue of whether an employee is entitled to the benefits of the provisions of this act. Any person aggrieved by the decision of the Industrial Accident Board may have a right of appeal to the Superior Court.

SECTION 8. *Physical examination.* The insurance company, self-insured employer or Industrial Accident Board shall be entitled to a physical examination of an employee receiving benefits under this act provided that such examining physician is duly licensed to practice in this commonwealth.

SECTION 9. *Assignment of rejected risks.* An employer who has been refused insurance under this act may appeal to the Insurance Commissioner, who shall make an equitable distribution of such refused risks among insurance companies authorized to write insurance under this act.

SECTION 10. *Benefits outside this act.* Any person who is entitled to workmen's compensation benefit, or unemployment compensation, shall not be entitled to the voluntary benefits of this act.

SECTION 11. *Effective date.* This act shall take effect on January 1, 1945.

DEATHS

VARNEY — Fred E. Varney, M.D., of North Chelmsford, died June 7. He was in his eighty-fourth year.

Dr. Varney received his degree from Bowdoin Medical School, in 1886. At the time of his retirement in 1936, the Massachusetts Medical Society honored him with the presentation of a medal commemorating fifty years' service to humanity.

His widow, a son, and a brother survive.

WATSON — Lester D. Watson, M.D., formerly of Milton, died June 14. He was in his forty-fourth year.

Dr. Watson received his degree from Boston University School of Medicine in 1928. He was formerly on the staff of the Milton Hospital and associated with the Massachusetts Memorial Hospitals. Recently he had been stationed on Long Island, New York, as assistant surgeon of the U. S. Public Health Service. He was a member of the American Medical Association and a fellow of the American College of Physicians.

His widow, two sons and a sister survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

EMERGENCY MATERNITY AND INFANT CARE PROGRAM

CONSULTANT SERVICE

A new standard for consultant service has been established in Massachusetts for the Emergency Maternity and Infant Care Program. A consultant paid under this program may be a diplomate in any

the usual course of the business of his employer and excepting domestic servants and farm laborers, shall be entitled to the voluntary benefits provided herein.

Section 2. *Present systems not affected.* Nothing herein shall be construed to affect any system in operation at the effective date of this act provided the benefits under such system equal the benefits provided herein and further provided that such system is approved by the Industrial Accident Board for the security of employees and any contract of insurance which is a part of such system shall be approved by the Insurance Commissioner as to the adequacy and reasonableness of premium charges and also as to form. Any person aggrieved by a ruling of the Industrial Accident Board or the Insurance Commissioner under this section may have a right of appeal to the Superior Court for a review thereof.

Section 3. *Election.* Any employee may elect to remain outside the provisions of this act provided he shall so notify his employer in writing within thirty days after the effective date of this act or if an employee is hired after the effective date of this act, then such notice shall be within ten days after his contract of hire. Any employee who has notified his employer of his election to remain outside the provisions of this act shall not be required to make any contribution by pay-roll deductions under this act.

Section 4. *Benefit.* Every employee who is unable to perform any services for wages because of his physical or mental condition, and has not given his employer notice in writing to remain outside this act, shall be entitled to the following specific benefits:

(a) *Cash sickness and bodily injury benefit.* Two thirds of the employee's average weekly wage but not to exceed \$20 per week. Payments to begin after two weeks' total disability because of physical or mental condition provided that a certificate from a duly licensed physician is procured to support the disability. The payments for one continuous disability shall be limited to twenty-six weeks.

(b) *Hospital benefit.* An employee shall be allowed for confinement in a legally chartered hospital expenses up to \$4 per day, not exceeding sixty days during each period of disability. The employee shall also be allowed up to \$20 for operating room, x-ray, laboratory and anesthetic fees. The employee shall have the right to choose a hospital of his own choice.

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JULY 13, 1944

Number 2

HODGKIN'S DISEASE*

II. Pathology

HENRY JACKSON, JR., M.D.,† AND FREDERIC PARKER, JR., M.D.‡

BOSTON

IN THE present paper there will be discussed the gross and microscopic features of the three types of Hodgkin's disease, the apparent site of origin in each and the extent to which each form involves the various organs of the body. Without some knowledge of the gross pathology and the distribution of the lesions one cannot hope to have a clear understanding of the clinical capacities of the disease.

HODGKIN'S PARAGRANULOMA

Hodgkin's paraganuloma appears to be a disease essentially of the lymph nodes. Those involved are most frequently found in the neck and are usually few in number, discrete, of rubbery consistence and not attached to the surrounding tissue (Table 1).

TABLE 1. *Apparent Primary Site of Disease in Cases of Hodgkin's Paraganuloma.*

	No OF CASES
Cervical lymph nodes	23
Inguinal lymph nodes	2
Axillary lymph nodes	1
Total	26

They are rarely more than 3 cm. in diameter and on cut section are yellowish gray. There is no evidence of softening or necrosis, and the capsule is intact.

On microscopic examination the normal structure of the lymph node as a whole is occasionally unaffected; more commonly it is partly or entirely lost. In some cases the lymph follicles are preserved and show only varying degrees and types of cellular activity; in others they are partly or completely obliterated. The peripheral sinus may be clearly outlined or be compressed by the follicles or obscured by actual cellular infiltration.

*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard) and the Mallory Institute of Pathology, Boston City Hospital, and the Department of Medicine, Harvard Medical School.

†Assistant professor of medicine, Harvard Medical School, associate physician, Thorndike Memorial Laboratory, Boston City Hospital

‡Associate professor of pathology, Harvard Medical School, pathologist-in-chief, Boston City Hospital.

The diagnosis is based on the presence, within the involved nodes, of Reed-Sternberg cells, which may be few or numerous. They occur especially in the pulp; more rarely they are seen in the lymph follicles. These large cells with multilobed or more rarely multiple nuclei and prominent nucleoli are indistinguishable from those found in the other forms of Hodgkin's disease. The cytoplasm is fairly abundant and tends to be amphophilic. Mitotic figures in the Reed-Sternberg cells of this form of Hodgkin's disease are not numerous.

The predominant cell of Hodgkin's paraganuloma is, however, the adult lymphocyte. In cases in which the lymph follicles have been obliterated, the diffuse infiltration of the nodes by lymphocytes may be so great that an erroneous diagnosis of lymphocytoma is easily made. Buried within this mass of lymphocytes are found, nevertheless, the typical Reed-Sternberg cell, for which a careful search must be made not infrequently. Reticulum cells, often containing phagocytosed debris, are present in varying numbers. In some cases they occur as focal aggregates resembling the lesions of Boeck's sarcoid. Plasma cells are not uncommonly seen and may be numerous. Eosinophils are sometimes present, but never in such quantities as in Hodgkin's granuloma.

The pathologic process never invades the capsule, although there may be an infiltration of this structure by scattered lymphocytes and plasma cells. In Hodgkin's paraganuloma one never sees the necrosis, the infiltration with polymorphonuclear leukocytes, the marked eosinophilia or the fibrosis so frequently found in Hodgkin's granuloma.

The changes in the reticulum vary widely. In some cases it is normal in amount; in others there is an increase in the number of fibers in the medullary cords but not in the follicles. In still others the fibers are thickened, but this change is usually associated with scarring due to some independent and unrelated process.

It should be pointed out that in certain cases of Hodgkin's paraganuloma the presence of fairly numerous eosinophils and fibrin is evidence that

a transformation into the granulomatous form is impending, and transitional types of the disease occur in which it is difficult to be sure whether one is dealing with Hodgkin's paraganuloma or with Hodgkin's granuloma. It may be argued that those cases of Hodgkin's paraganuloma that fail to change into Hodgkin's granuloma represent, indeed, an entirely different disease. It must be remembered, however, that those that progress cannot, in their incipency, be distinguished from those that do not. For instance, in 1910 one of our patients had a cervical lymph node removed that showed the typical picture of Hodgkin's paraganuloma. Subsequent biopsies from the neck in 1917 and 1936 showed a histologic picture indistinguishable from that seen in 1910. The patient has continued to be in good health to date. On the other hand, a second patient in 1941 had a cervical lymph node removed that showed the typical histologic picture of Hodgkin's paraganuloma. He was given a moderate amount of high-voltage x-ray treatment and continued in apparently good health until 1943, at which time he suddenly became progressively worse, with all the signs and symptoms usually associated with advanced Hodgkin's granuloma. Autopsy showed extremely extensive involvement with the granulomatous type of the disease. The initial biopsy specimens from these two cases were indistinguishable. In the first case, the type of lesion did not alter over a period of twenty-six years, and the patient was alive and active thirty-eight years after the initial lymphadenopathy had been noted. In the second case, on the other hand, the histologic picture changed with considerable rapidity and death shortly ensued. A third patient had a large mass of nodes dissected from the neck in 1920. He remained active and in apparent good health until 1943, when he returned with a large mediastinal mass and a few lymph nodes in the neck. These proved on biopsy to be Hodgkin's granuloma. In 3 other cases, Hodgkin's granuloma developed as proved by autopsy. Four patients died of unrelated causes such as carcinoma or tuberculosis, and 5 died from causes unknown. Unfortunately, no autopsy was obtained in any of the latter cases. Thirteen patients are alive and active, although some still show evidence of their disease.

It should be emphasized that so long as the pathologic process remains unaltered the prognosis is relatively good, but in certain cases Hodgkin's granuloma develops, and the prognosis then becomes that of the latter condition.

If the pathologic process remains that of Hodgkin's paraganuloma, involvement of the internal organs appears to be rare. In 4 cases, the mediastinal nodes became involved. Three of these patients are still alive, and 1 died of pulmonary tuberculosis. In 2 cases, the spleen became definitely enlarged. Each of these patients died at home of

unknown causes. In 3 cases, both the mediastinal nodes and spleen became involved. All these patients have died. There were no autopsies.

HODGKIN'S GRANULOMA

The granulomatous process may involve isolated groups of nodes in certain regions, or the process may be widespread. In our series of cases, the lymph nodes were implicated to some extent in every case. Cases have been reported, however, in which the disease was confined to a single organ with no lymph-node involvement, such as the 2 cases mentioned by Sternberg¹ in which the spleen alone was diseased.

From autopsy studies of 59 cases, it is shown that the retroperitoneal and para-aortic lymph nodes were the most frequent primary site of the disease, followed by other lymph nodes and the stomach or intestines (Table 2). This is in sharp contrast to

TABLE 2. Primary Site of Disease in Cases of Hodgkin's Granuloma.

SITE	No. of Cases
Lymph nodes	53
Retroperitoneal	17
Para-aortic	13
Mediastinal	9
Cervical	8
Mesenteric	6
Gastrointestinal tract	6
Stomach	3
Duodenum	1
Small intestine	1
Large intestine	1
Total	59

the clinical observations, from which it appears that the cervical nodes were the primary site in an overwhelming percentage of the cases. It is probable that the favorable response of the more superficial nodes to x-ray therapy and the difficulty of recognizing during life involvement of the deeper nodes and internal organs account for this apparent discrepancy. But the fact that internal lymph nodes are so frequently involved at autopsy and primarily so, even though they have been suspected of being implicated during life, should make the physician cautious before deciding, in a given case, that the disease is confined to a small number of obviously involved but comparatively localized superficial nodes.

The diseased lymph nodes often occur in masses, but the outlines of each can usually be made out. Their consistence may be soft or firm, but with deposition of connective tissue the nodes become increasingly harder. Only rarely, however, do they assume the stony hardness so suggestive of carcinoma. The cut surface is grayish white, often with a brownish tint. It may be homogeneous or may show foci of necrosis, which are of varied shape and are white to yellow. In our experience, breaking down or softening due to Hodgkin's granuloma alone does not occur. Secondary in-

fection, particularly in the groin, may, however, give rise to abscess formation or the deposition of scar tissue to such an extent that a definitive diagnosis is impossible. If feasible, it is always wise to avoid the removal of a node from the groin and to choose for biopsy a lymph node in the neck or axilla, provided that there is one of sufficient size and that it is readily accessible.

The histologic picture of Hodgkin's granuloma is characterized by the presence of Reed-Sternberg cells and by its great pleomorphism. The lymph nodes involved as a rule show complete loss of their normal architecture. The germinal centers and the cords of lymphatic tissue as well as the sinuses are obliterated. Extension of the process into the capsule may occur. It must be remembered that in any given case the histologic picture in the nodes in different regions or even in different nodes in the same region may vary widely.

The typical Reed-Sternberg cell measures from 12 to 40 microns in diameter. Its shape is often irregular, and cytoplasmic processes frequently extend between neighboring cells. The nucleus, in its most characteristic form, is lobulated or multilobed. Multinucleated forms also are seen. Small forms of the Reed-Sternberg cell may occur, and in these the nucleus is round or oval. The chromatin occurs in heavy clumps, and large nucleoli are a prominent feature. The cytoplasm, which is abundant in proportion to the nucleus, varies in its staining reaction from acidophilic to basophilic, tending to be basophilic in the younger forms. In sections of tissue fixed in Zenker's fluid and stained with Mallory's phloxin-methylene blue stain, the cytoplasm often appears finely reticulated.

In sections stained for reticulum, the Reed-Sternberg cells often contain numerous silver-positive granules. In such sections these cells are often found closely applied to the reticulum fibers, and in some cases these fibers seem to pass through the cytoplasm. When stained with Penfield's modification of Hortege's silver carbonate method for microglia, the Reed-Sternberg cells tend to become impregnated, as do phagocytes of mesenchymal origin, as shown by Dunning and Furth² and as noted by us in unpublished studies. As a general rule, there is an increase in the number of reticulum fibers, which either run between single cells or enclose groups of cells. As sclerosis advances, the fibers tend to be thicker and more numerous. In a completely fibrosed node, the major portion of the intercellular substance is dense collagen.

Mitotic figures are not uncommon, and multiple mitoses are occasionally seen. Phagocytosis by Reed-Sternberg cells is uncommon. There is a strong tendency, however, for them to undergo necrobiosis. Thus, in a section of Hodgkin's granuloma scattered degenerating and pyknotic Reed-Sternberg cells are frequently found, and this feature is often an aid in diagnosis when one may be in

doubt whether true Reed-Sternberg cells are present.

In supravital preparations, the cytoplasm has a ground-glass appearance, and in some cells a delicate, finely granular rosette stained with neutral red can be seen in close proximity to the nucleus.

The exact origin of the Reed-Sternberg cells has not been proved, but we agree with those workers who believe that they are derived from the sinus endothelium and from reticulum cells. In favor of such an origin is their resemblance to these cells, especially when the Reed-Sternberg cells are small and mononuclear. A more striking resemblance is seen in the cells of Hodgkin's sarcoma and of anaplastic reticulum-cell sarcoma, in which the differential diagnosis must rest on the presence or absence of Reed-Sternberg cells. It is, of course, extremely important to differentiate normal reticulum cells and Reed-Sternberg cells. When the latter are large and typical, no difficulty should be encountered. When, however, they are small and the nuclei are not multilobed, the differential diagnosis depends on the character of the nucleus. The nucleus of a reticulum cell has finely divided, scattered chromatin and lacks a prominent nucleolus, whereas a Reed-Sternberg cell has its chromatin arranged in large masses and is characterized by one or more prominent nucleoli.

Cells occasionally confused with Reed-Sternberg cells are multinucleated plasma cells, foreign-body giant cells, Langhans giant cells, tumor giant cells and megakaryocytes. The last two may present great difficulties in differential diagnosis. Tumor giant cells, however, rarely occur singly as do Reed-Sternberg cells, and they are accompanied by other tumor cells characteristic of the neoplasm at hand. Foreign-body giant cells and Langhans cells have nuclei varying in number from several to twenty or more, and the nuclei in each of these types of cells are regular in shape, equal in size and orderly in arrangement. The chromatin is finely divided, and nucleoli are not prominent. Megakaryocytes closely resemble Reed-Sternberg cells, and given a single cell it is almost impossible to determine which of the two it is, although megakaryocytes do not have prominent nucleoli and their nuclei, although multilobed, are always single. The diagnosis must therefore depend on the picture of the section as a whole. To illustrate the difficulty of a definitive diagnosis, we refer to a nodule in the skin removed from a patient with proved myelogenous leukemia. Megakaryocytes were a prominent feature, and a number of highly competent pathologists without hesitation diagnosed the disease as Hodgkin's granuloma.

The nature and significance of the Reed-Sternberg cell is entirely obscure. It has been considered a tumor giant cell by those who consider Hodgkin's granuloma a neoplasm. In our opinion, it is probably a peculiar reactive form of the reticulum cell

in response to the agent causing the disease. In support of this conception is the cellular reaction to infection with *Bacillus mallei*, in which, as is well known, a characteristic type of giant cell is seen. It is our opinion that in like manner the Reed-Sternberg cell of Hodgkin's granuloma is the response to the unknown etiologic agent of that disease.

The number of Reed-Sternberg cells in granulomatous nodes varies widely. In some they are few in number; in others they are numerous, and may occur in groups as well as scattered. Rarely if ever are they so scarce as in paraganuloma.

In addition to the Reed-Sternberg cells, there are many other types of cells, and a pleomorphic picture is indeed characteristic of the disease. Lymphocytes are usually numerous. Plasma cells are almost constantly present, their number varying from a few to so many that a diagnosis of plasmacytoma may be entertained. One of the most outstanding features of the histologic picture of Hodgkin's granuloma, as first pointed out by Goldmann,³ is the presence of eosinophils. They are practically always present, although their number varies widely. In addition, polymorphonuclear neutrophilic leukocytes can usually be found, and are particularly prominent when the inflammatory reaction is extremely active and necrosis is present. Activity on the part of the reticulum cells, as evidenced by hyperplasia and hypertrophy, is frequent, sometimes with the formation of focal lesions resembling tubercles or Boeck's sarcoid.

In addition to the pleomorphic cellular content, two other changes are found that are characteristic of the granuloma—necrosis and fibrosis. The necrosis varies in extent from minute microscopic foci to large areas easily visible grossly. It is often of the infarct type, the cell outlines being preserved in the necrotic area. Polymorphonuclear leukocytes and reticulum cells may be found at the periphery of necrotic areas. Fibrin formation is common. Occasionally giant cells of the foreign-body type are present. The necrotic areas are eventually organized by the ingrowth of the fibroblasts of the stroma. As the processes of necrosis and fibrosis proceed, some lesions finally come to be largely composed of connective tissue, often dense and sometimes hyaline, in the interstices of which can be seen a few Reed-Sternberg cells. A high degree of fibrosis does not necessarily mean a long-standing process; on the contrary, it may represent a favorable reaction on the part of the host. Several patients when first biopsied have shown such a picture in their nodes, and their subsequent course has been relatively favorable.

As is well recognized, radiation therapy produces a high degree of sclerosis. In such nodes, however, even though markedly fibrosed, an occasional Reed-Sternberg cell can always be found.

The lesions described above may vary considerably in the different organs or tissues of any given patient. For example, some lesions present a marked inflammation with but little necrosis, others show extensive necrosis, and in still others fibrosis is the outstanding feature. The type of histologic picture depends presumably on such factors as the activity of the process, the age of the lesion and the reaction of the host to the causative agent.

Occasionally, as Sternberg¹ has pointed out, large amounts of lipid are found in the reticulum cells and in giant cells of the foreign-body type. The significance of this phenomenon is not clear, but that it may occur must be recognized in order to avoid the error of making a diagnosis of one of the diseases of disturbed lipid metabolism, such as Niemann-Pick's disease or Gaucher's disease, and of overlooking the essential granulomatous lesion.

Some authors have described another feature as not uncommon, namely, amyloid formation. In our experience this has been extremely rare.

The granulomatous form of Hodgkin's disease is frequently associated with active tuberculosis. It has been said that tuberculosis follows Hodgkin's disease like a shadow. The two processes may exist side by side in the same organ, and although grossly one may be confused with the other, the histologic characteristics of each are so definite that no difficulty in distinguishing them should be encountered.

The lymph nodes were involved at autopsy in every case in this series, and it is noteworthy that the involvement was usually widespread and of fairly uniform distribution (Table 3).

Aside from the generalized lymphadenopathy, almost every organ of the body with the exception

TABLE 3. *Lymph Nodes Found to Be Involved at Autopsy in 59 Cases of Hodgkin's Granuloma.*

TYPE OF NODE	NO. OF CASES
Mediastinal	55
Para-aortic	34
Cervical	30
Retroperitoneal	28
Mesenteric	28
Inguinal	25
Axillary	25

of the central nervous system proper may be invaded (Table 4). This fact accounts for the extraordinarily protean clinical manifestations.

The spleen is involved in a large percentage of cases. In Sternberg's¹ series it showed lesions in 80 per cent, in Terplan's⁴ in 65 per cent, and in Uddström's⁵ in 63 per cent. In our series it was involved in 75 per cent. The involved organ may be normal in size or enlarged to a marked degree. The largest spleen in this series weighed 1245 gm. and the smallest 120 gm., with an average of 480 gm. The lesions appear as circumscribed focal areas, gray to yellowish and varying in diameter from that of a miliary tubercle to a centimeter or more. As a rule, the

lesions in each spleen are of approximately the same size. Foci of necrosis similar to those seen in lymph nodes may occur. The picture produced by the focal lesions contrasting with the red color of the uninvolved portion has led to the terms "porphyry"⁶

TABLE 4. *Organs Found to Be Involved at Autopsy in 59 Cases of Hodgkin's Granuloma*

ORGAN	NO OF CASES
Lymph nodes	59
Spleen	44
Liver	51
Bones*	27
Vertebra	25
Sternum	3
Rib	3
Ilium	2
Femur	1
Skull	1
Lung	24
Pleura	10
Infiltration only	5
Effusion only	3
Infiltration and effusion	2
Gastrointestinal tract	10
Stomach	4
Small intestine	4
Duodenum	1
Cecum	1
Peritoneum	10
Ascites only	9
Ascites and infiltration	1
Kidneys	8
Pancreas	8
Pericardium	8
Effusion only	6
Infiltration only	2
Adrenal glands	7
Diaphragm	3
Uterus	2
Breast	2
Skin	2
Thyroid gland, trachea, aorta, ovary, bladder	1 each

*Multiple involvement

and "Baueruurst"⁷ spleen. The spleen has been described as the sole site of the disease.¹ In our series other organs were always involved.

Histologically, the lesions in the spleen resemble those in the lymph nodes.

The liver is frequently affected. It was involved in 38 per cent of Sternberg's cases and in 53 per cent of our series. Massive enlargement of the liver is in our experience rare. The largest liver weighed 3500 gm. In 29 of the 59 autopsied cases the organ weighed more than 1800 gm., and in 18 of these foci of Hodgkin's disease were noted. On the other hand, of the 16 livers weighing less than 1600 gm. only 4 were involved. The focal, circumscribed nodules are similar to those in the spleen, or there may be grayish streaks of diseased tissue following the distribution of the portal areas. If fibrosis is extensive, scars may be produced in such a manner that healed gummas are simulated. Some authors have described the lesions as resembling those of cirrhosis. Bile stasis due to compression of the bile ducts by the surrounding granulomatous tissue, resulting in jaundice, does occur, but it is rare. The small lesions tend to occur in the portal areas. Their histologic composition and pattern are similar to those of the lesions in lymph nodes. The large foci may cause compression and destruction of the surrounding liver tissue.

Statistics concerning the incidence of involvement of bones in Hodgkin's granuloma are unsatisfactory because of the incompleteness of examination of the osseous system.⁸ In a recent review of Hodgkin's granuloma with special reference to the involvement of the bone marrow, Steiner⁹ collected from the literature 547 autopsied cases, of which 153 (28 per cent) showed lesions of the bone marrow. In his own 14 cases, he found the marrow involved in 11 (78 per cent); it should be pointed out that he examined sixty-two bones in the 14 cases. In our series involvement of the bones occurred in 61 per cent of those cases in which the osseous system was examined. Such a figure is, however, obviously inaccurate because of the limitations in making a thorough gross and microscopic study of the bones in each case. The bones most commonly involved at autopsy in order of their frequency are the vertebrae, especially the lower thoracic and upper lumbar, and much more rarely the sternum, ribs, pelvis, femur and skull. Multiple involvement is not uncommon. The lesion may be confined to the marrow, or the process may invade and destroy the cortex, leading in the case of the vertebrae to collapse, which if extensive may result in compression of the cord, although it is surprising to what extent collapse can occur without clinical symptoms. Involvement of the bones may be metastatic or by extension from neighboring organs. Grossly the lesions appear as grayish to yellowish nodules that stand out against the remnants of the normal marrow. Although fibrosis of the involved marrow often occurs, osteosclerosis is rare.

Histologically, the lesions may be miliary in type, composed of typical granulomatous tissue with but little disturbance of the bony architecture, or extensive, causing destruction of the bony trabeculae. The process replaces the normal marrow, and at the periphery of the process great activity on the part of the hematopoietic tissue may be present. In a specimen of marrow removed by biopsy, unless a certain degree of fibrosis is present, great difficulties may be encountered in making a definite diagnosis because of the similarity of the megakaryocytes to Reed-Sternberg cells.

Versé¹⁰ estimated from a study of his own material and from the cases reported in the literature that approximately one third of the cases show involvement of the lungs. Sternberg¹ stated that of his 52 autopsied cases, 15 (29 per cent) showed such lesions. Pulmonary involvement was found in 41 per cent of our cases. The lesions may be divided into three types. In the first type, there appears a large, tumorlike mass, often involving the greater part of a lobe. Such a condition may easily be mistaken, both by x-ray and grossly at autopsy, for bronchiogenic carcinoma. In the second type, grayish streaks of diseased tissue follow the course of

in response to the agent causing the disease. In support of this conception is the cellular reaction to infection with *Bacillus mallei*, in which, as is well known, a characteristic type of giant cell is seen. It is our opinion that in like manner the Reed-Sternberg cell of Hodgkin's granuloma is the response to the unknown etiologic agent of that disease.

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of the central nervous system proper may be invaded (Table 4). This fact accounts for the extraordinarily protean clinical manifestations.

The spleen is involved in a large percentage of cases. In Sternberg's¹ series it showed lesions in 80 per cent, in Terplan's⁴ in 65 per cent, and in Uddstromer's⁵ in 63 per cent. In our series it was involved in 75 per cent. The involved organ may be normal in size or enlarged to a marked degree. The largest spleen in this series weighed 1245 gm. and the smallest 120 gm., with an average of 480 gm. The lesions appear as circumscribed focal areas, gray to yellowish and varying in diameter from that of a miliary tubercle to a centimeter or more. As a rule, the

series there was a moderate (100 to 300 cc.) serous effusion.

Twelve per cent of our cases showed involvement of the adrenal glands. In each case there had been extension of the granulomatous process from adjacent lymph nodes. Sternberg's experience was similar.

The uterus was involved microscopically in 2 of our cases.

Implication of the ovaries is rare. In 1 of our cases there was a microscopic lesion.

Sternberg¹ reports 2 cases of Hodgkin's granuloma of the thyroid gland. In 1 of our cases there were metastatic lesions in this organ.

In none of our cases was the prostate gland involved; Sternberg mentions 1 case reported in the literature. No involvement of the testis or epididymis was found, although a rare case has been described in the literature.⁴

Sternberg found granuloma of the tonsil in 5 of his 52 cases. The tonsils were enlarged and ulcerated. In none of our cases were the tonsils involved.

Rarely there is invasion of the diaphragm, breast, skin and certain other organs (Table 4).

Lesions of the central nervous system proper do not occur. Compression of the cord due to extradural masses or periosteal infiltrations of the vertebrae, however, is not infrequent. In our series no case showed such lesions at autopsy. Clinical evidence of meningeal involvement is, however, not uncommon. It should be mentioned that patients with Hodgkin's granuloma may show signs and symptoms indicating cerebral involvement, yet at autopsy no demonstrable anatomic change can be found. During life 1 of our patients had extraordinary disturbances of taste and complete anorexia, yet extremely prolonged and careful examination of the nervous system failed to reveal even a microscopic lesion.

HODGKIN'S SARCOMA

Studies of 27 autopsied cases show that Hodgkin's sarcoma usually has its origin in the retroperitoneal lymph nodes and that the lesion is characteristically invasive and destructive.

The disease was primary in the retroperitoneal nodes in 19 (70 per cent) of our cases (Table 5), and

TABLE 5. *Apparent Primary Site of Disease in Cases of Hodgkin's Sarcoma.*

	No of Cases
Retroperitoneal lymph nodes	19
Stomach .	3
Tonsil	2
Mediastinal lymph nodes	1
Para-aortic lymph nodes	1
Lung	1
Total . .	27

in all the involvement was extensive and extremely destructive. In 1 case, there was a retroperitoneal

mass of confluent lymph nodes weighing in the aggregate 1600 gm. and direct extension from these nodes to the second and third parts of the duodenum, the stomach, the head of the pancreas and the lower surface of the liver. In addition, there was compression of the common bile duct, and the aorta was buried in and partially compressed by a mass of firm, elastic nodes extending from the diaphragm to the bifurcation of the iliac vessels. In another case, a mass of lymph nodes extended along the entire length of the abdominal aorta, and the tumor infiltrated the right psoas and the right latissimus dorsi muscles, filled the entire right abdominal gutter and extended from deep within the pelvis to the twelfth right rib, which was compressed and eroded by the tumor. In a third patient, the lymphadenopathy extended from the level of the pancreas into the true pelvis.

Of the remaining 8 cases, the disease was primary in the stomach in 3, in the tonsil in 2, and in the lung, mediastinum and para-aortic nodes in 1 each. The lymph nodes were involved to a varying degree in every case, and peripheral lymphadenopathy was not uncommon (Table 6).

As might be expected, the retroperitoneal tumors resulted in many complications, such as hydro-

TABLE 6. *Lymph Nodes Found to Be Involved at Autopsy in 27 Cases of Hodgkin's Sarcoma.*

TYPE OF NODE	No of Cases
Retroperitoneal	21
Mediastinal	14
Mesenteric	12
Axillary .	11
Cervical .	10
Inguinal	9
Para-aortic	4

nephrosis, obstruction of the common bile duct and venous thrombosis due to compression by or invasion from adjacent tumor. The tendency to invade neighboring structures such as the pancreas, adrenal glands and muscle was marked.

The involved nodes were enlarged, often greatly so. In some cases their outlines could be recognized; in others the tumor had invaded the capsule, resulting in a large, irregular-shaped conglomerate mass. In consistence, the tumor may be fairly firm or soft or even practically diffuent. As a rule, however, the tissue cuts with ease, and the cut surface is grayish white to white. Areas of necrosis are not infrequent, and appear as yellowish foci that may be extremely small or very extensive.

Histologically, the tumor is composed of cells two or three times the size of a normal lymphocyte. The nucleus is usually round but may be ovoid. The majority of the cells have single spherical nuclei with prominent nucleoli, but Reed-Sternberg cells with multilobed nuclei are always seen. Their presence is necessary to establish the diagnosis of Hodgkin's sarcoma. These cells vary in number considerably from case to case, being numerous in some and few

the bronchi and usually represent an extension from affected mediastinal and tracheobronchial lymph nodes. Invasion of the walls of the bronchi with compression or even occlusion of their lumens may occur. In the third and rarest type, there are small to medium-sized circumscribed nodules scattered diffusely through the parenchyma.

Histologically, the process shows wide variations. The granulomatous tissue may fill the alveoli without destroying their walls; on the other hand, the normal structures may be entirely destroyed and replaced by the granuloma. In some cases very little connective tissue is present, the alveoli, however, containing numerous Reed-Sternberg cells. Such a cellular type of lesion may be confused with Hodgkin's sarcoma, but in the lymph nodes and other organs from the same case the usual typical granulomatous process is present and post-mortem diagnosis is not difficult. In other cases fibrosis is such an outstanding feature that the lesion resembles an organized pneumonia and careful search is necessary to detect Reed-Sternberg cells lying in the interstices of the dense connective tissue. All variations between the distinctly cellular type of process and the highly fibrotic are encountered. Cavity formation is rare and probably represents, when it does occur, a pyogenic infection of the granulomatous tissue, although in some cases, if a bronchus has been occluded, it is of the nature of a bronchiectatic abscess. The formation of lesions beneath the visceral pleura is not uncommon. The pleura is reported by Sternberg¹ as being occasionally involved. In 5 of our autopsied cases there was infiltration of the pleura without effusion, in 3 there was serous effusion only, and in 2 there was serous effusion together with infiltration of the pleura. In no case was the effusion bloody. In every case in which there was effusion the mediastinal nodes were involved.

Hodgkin's granuloma in the gastrointestinal tract may be either primary or secondary. The secondary type is usually the result of the invasion from adjacent diseased lymph nodes or other organs. In addition, secondary lesions appear as nodules in the serosa or mucosa as the result of metastasis from a generalized granulomatous process.

In our series of autopsies there were 6 cases of Hodgkin's granuloma primary in the gastrointestinal tract. Three were primary in the stomach, 1 in the ileum, 1 in the duodenum and 1 in the cecum. These figures are in essential agreement with those of Sternberg.

Grossly the gastric lesion may appear as a polypoid, tumorlike mass projecting into the lumen or as a broad-based ulcer with firm raised edges. It may lead to thickening of practically the entire wall, with marked accentuation of the normal rugae. This probably gives rise to the so-called *Gehirnaspekt* in x-ray films of the stomach, considered by some as

diagnostic of the disease. There is usually extension to neighboring lymph nodes. In rare cases only the local gastric lymph nodes are involved and no other organs or tissues show evidence of the granulomatous process.

Microscopically, the lesions in the stomach vary considerably. In some cases the process is composed of numerous Reed-Sternberg cells, many eosinophils and some lymphocytes and plasma cells, with little or no fibrosis. In other cases the granulomatous infiltration shows a moderate or a marked degree of fibrosis in addition to the characteristic cytologic elements. If there has been ulceration, the picture is further complicated by superficial necrosis and the presence of numerous polymorphonuclear leukocytes.

According to the literature,^{11,12} the intestinal granulomatous process is most frequently situated in the duodenum or the jejunum. In our series there were lesions in the lower small intestine in 4 cases, in the duodenum in 1 and the cecum in 2. The lesions appear as flat ulcers with raised, rather firm edges and with irregular, granular bases. The bowel wall may be entirely encircled. The granulomatous process also appears as plaques or tumorlike nodules that may obstruct the lumen and lead to intussusception. Cases have been reported in which erosion of an artery at the base of a granulomatous ulcer has resulted in a fatal hemorrhage. In 1 of our cases, not included in the autopsy series because there was only an incomplete post-mortem examination, rupture of the small intestine resulted in the sudden death of a patient who had appeared the day before to be in excellent condition. The possibility of such sudden deaths must always be borne in mind. Microscopically, the lesions resemble those found in the stomach.

In 9 of our autopsied cases there was marked ascites, in only 1 were there actual lesions in the peritoneum. In all cases having ascites there was involvement of the retroperitoneal nodes.

Involvement of the kidneys when the granulomatous process is widespread is not unusual. In our series it occurred in 14 per cent of the cases. There are usually small circumscribed nodules, situated especially in the cortex. We agree with Sternberg that massive lesions are distinctively rare. The histologic picture needs no comment. The ureters may be affected by extension of the process from neighboring lymph nodes.

Secondary involvement of the pancreas by extension of granulomatous lesions of the stomach, small intestine or retroperitoneal nodes is not very uncommon; it occurred in 8 of our cases. Primary involvement was not found, although it has been described in the literature.¹³

The heart muscle was not invaded in any case, but in 2 cases there were small nodules on the parietal pericardium. Terplan and Mittelbach⁴ report such lesions as being frequent. In 6 other cases in our

however, was secondarily involved in 8 cases, chiefly by metastasis. The lesions appeared as grayish-white nodules of varying size and number and were situated in the mucosa. In 2 cases the large intestine showed metastatic nodules in the mucosa, and it was invaded by extension of a primary tumor of the retroperitoneal lymph nodes in 2. In 1 case, there was a microscopic lesion of the esophagus.

It should be particularly noted that involvement of the gastrointestinal tract was not infrequently multiple and often extensive.

The pancreas was affected by tumor in 11 cases (41 per cent). In 1, the tumor was apparently metastatic from a primary lesion of the tonsil. The other cases represented direct extension from primary tumors of neighboring structures — the stomach in 3 cases and the retroperitoneal lymph nodes in 7.

The bones were examined in 22 cases. Ten of these showed tumor. In 7 cases, the vertebrae were involved, the tumor appearing as grayish nodules surrounded by red, uninvolved marrow. In 3 cases, the skull had been invaded, twice by direct extension from tumors primary in the tonsil. In the first of these, there was a pedunculated growth on the superior part of the occipital bone. The region of the sella was markedly widened, and the pituitary was involved by soft, grayish tissue. The bony structures surrounding the fossa were softened. The tumor also occupied the entire sphenoidal sinus, had eroded the surrounding sphenoidal structures and was found as well in the foramen lacrum of the petrous portion of the temporal bone. In the second case, the tumor invaded and partly destroyed the antrum and bones of the orbit on one side. In the third case, involvement of the skull was apparently metastatic from the retroperitoneal lymph nodes. In the region of the right temple there was a superficial swelling of the scalp 8 cm. in diameter. The inner table of the skull beneath this was shaggy, and the entire thickness of the bone was involved by tumor that had extended through to the dura, which was diffusely invaded. There was, however, no extension to the pia-arachnoid.

There was 1 case of involvement of the great trochanter of the femur. In 2 cases, the tumor, primary in the retroperitoneal nodes, had extended directly to the pelvic bones. In another case, the ribs showed multiple tumors secondary to a primary lesion of the para-aortic lymph nodes.

Ten cases showed involvement of the lungs at autopsy. In 1, the tumor was primary in the right lower lobe, and owing to the extensive involvement and the apparently abrupt onset, the case on admission was mistaken for one of lobar pneumonia. At autopsy, the grayish-white tumor occupied practically the whole of the lower lobe and was necrotic in its center. In 2 cases, there were scattered nodules approximately 1 cm. in diameter. Two cases grossly showed no visible tumor but it was present micro-

scopically. In the other 5 cases, the tumor had extended in from the mediastinal nodes along the bronchi.

The adrenal glands were involved in 9 cases, in each by direct extension from tumors arising in adjacent lymph nodes.

The spleen was involved in 9 cases, much less often — and far less extensively — than in Hodgkin's granuloma. In 1 case, there was direct extension from a tumor primary in the retroperitoneal lymph nodes, in the form of a yellow-white mass extending in from the hilus in a radial manner for some 6 cm. The splenic artery and vein were surrounded by the neoplasm but were not invaded by it. In 2 cases, the spleen showed only microscopic lesions. In the remaining cases there were one or more grayish-white nodules, varying in diameter from 0.1 to 1.0 cm. The involved spleens were uniformly but not greatly enlarged, the heaviest of them weighing 640 gm.

The kidneys were involved in 8 cases, in each of which the tumors were metastatic. In no case did they result from invasion from surrounding structures. In every case each kidney was involved to a similar degree. The tumor nodules were less than 1 cm. in diameter and were usually situated in the cortical region.

There was invasion by tumor of the muscles of the thoracic wall in 1 case, of the psoas muscle in 2, of the quadriceps in 1, and of the diaphragm in 1.

The central nervous system was involved in 15 per cent of the autopsies. Again one sees the sharp contrast between Hodgkin's sarcoma and Hodgkin's granuloma, in which, so far as we are aware, no involvement of the central nervous system proper has been reported. In 1 case, the tumor was primary in the paravertebral lymph nodes and had extended between the transverse process of the vertebrae from the third cervical to the eleventh dorsal, invading the dura and causing marked compression of the spinal cord in the upper cervical region. In another, there was a metastasis from a primary tumor of the retroperitoneal lymph nodes to the cerebellum. This was described as a ridge of tumor measuring 5 by 3 by 0.5 cm. and extending along the superior surface of the cerebellum. Microscopic examination revealed extensive invasion of the cerebellum well into the dentate nucleus.

The pituitary gland was involved in 3 cases. In 1 case, in which the tumor was primary in the tonsil, the gland was invaded and its normal structure obliterated. In another, it was surrounded and compressed by neoplastic tissue but was not actually invaded. In the third, microscopic examination revealed invasion of the capsule and the peripheral portion of the pars nervosa; the tumor was primary in the retroperitoneal lymph nodes.

In 3 cases, there was a moderate serous effusion into the pericardial sac, and in another a small nodule of tumor was seen in the parietal pericardium itself.

and far between in others. It is our belief that the cells with a single spherical nucleus are undifferentiated forms of the Reed-Sternberg cell. This theory is sustained by the staining reactions, the character of the chromatin and the presence of transitional forms. The cytoplasm of the tumor cells tends to stain neutrophilic or basophilic. When stained with Mallory's phloxine-methylene blue, after Zenker fixation, the cytoplasm often has a granular or reticulated appearance. Mitotic figures are usually numerous, as would be expected in a highly malignant tumor.

Apart from the tumor cells, there are usually only scattered lymphocytes and reticulum cells. The former are readily identifiable by their comparatively small size and the characteristically dense masses of chromatin. Reticulum cells are easily recognizable by their finely divided, scattered chromatin and acidophilic cytoplasm. Neutrophils, eosinophils and plasma cells are rarely found unless the tumor is located in a region exposed to complicating inflammatory infiltration. Areas of necrosis, usually of the infarct type, are not infrequent. It should be emphasized that the diagnosis of Hodgkin's sarcoma rests, in the last analysis, on the presence of Reed-Sternberg cells.

With silver stains, the reticulum fibers are usually found to be increased in number. They enclose groups of cells as well as single cells. In some cases the fibers are not only more numerous but also somewhat thickened.

The structure of the affected node is destroyed by the diffuse growth of the tumor cells. The capsule may be intact or may be extensively invaded, with extension of the neoplasm into the surrounding tissues.

Aside from the lymph nodes, the organs most frequently involved in our series were the liver, the gastrointestinal tract, the pancreas, the bones and the lungs (Table 7). The liver was involved to a greater or less degree in 16 cases (59 per cent). In 10 of these, the tumor occurred as grayish-white nodules scattered throughout the parenchyma. The size of such nodules varied widely from case to case, but in each case they were of approximately the same size. The smallest foci averaged 2 mm. in diameter and the largest measured several centimeters. In some cases only two or three tumor nodules could be found, whereas in others the organ was studded with them. In 3 cases, the tumor was situated only in the capsule. In 3 cases, there was direct extension into the liver, either from the stomach or from the retroperitoneal nodes.

On the whole, the liver was somewhat enlarged, the largest weighing 2900 gm., but the majority weighed approximately 2000 gm., and it is notable that in a number of cases the liver, although definitely involved, was no larger than normal, the few metastatic nodules being buried deep within its substance.

Various portions of the gastrointestinal tract were involved in 15 cases (55 per cent). This is in sharp contrast to the comparatively uncommon involvement of the gastrointestinal tract in Hodgkin's granuloma. In 3 cases, the disease was primary in the stomach. In one of these, the tumor involved

TABLE 7 *Organs Found to Be Involved at Autopsy in 27 Cases of Hodgkin's Sarcoma.*

ORGAN	No OF CASES
Lymph nodes	27
Liver	16
Gastrointestinal tract*	15
Stomach	8
Small intestine	4
Duodenum	4
Colon	4
Esophagus	1
Pancreas	11
Bones*	10
Vertebrae	7
Skull	3
Pelvis	2
Ribs	1
Femur	1
Lungs	10
Adrenal glands	9
Spleen	9
Kidneys	8
Muscles	5
Central nervous system	4
Pituitary gland	3
Cerebellum	1
Pericardium	4
Gall bladder	3
Thyroid gland	2
Tonsil	2
Testicle	2
Ovary, uterus, iliac vein, bladder and dura	1 each

*Multiple involvement

the posterior wall in its middle third, extending from the greater to the lesser curvature and causing an ulceration over an area measuring 12 by 4 cm. There was considerable erosion at the base of the ulcer, and extensive hemorrhage had taken place from it. The tumor was white and necrotic and cut easily. In another case, the tumor appeared as a craterlike ulcer, 4 cm. in diameter, situated 2 cm. above the pylorus. The edges of this area were elevated 0.3 to 0.4 cm. above the surrounding mucosa and were made up of moderately firm, white tissue. The center of the crater was soft and homogeneous. On section, the tumor was found to extend into the pancreas and between the vertebral bodies. In the third case, the tumor occurred at the cardiac end of the stomach and involved an area 14 cm. in diameter. From the mucosal aspect, the neoplasm appeared as a plateaulike elevation, one portion of which was cauliflowerlike, and measured 4 cm. in diameter; the surface was ulcerated and greenish gray. The tumor tissue was homogeneous, pinkish gray and soft.

In 5 other cases, the stomach was secondarily involved. In one, the tumor appeared as an ulcer; in another, as raised patches in the mucosa. In a third, the stomach wall was invaded by primary tumor of the retroperitoneal nodes. In the other two cases, the tumor produced no visible macroscopic change.

There were no tumors primary in the small or large intestine. The small intestine or duodenum,

TABLE 1. The Concentration of Various Constituents in the Blood Serum of Patients with Pemphigus.

TYPE OF DISEASE	PATIENT	DATE	TOTAL BASE	SODIUM	POTASSIUM	CALCIUM	CHLORIDE	PROTEIN	PHOSPHATE	NON-PROTEIN NITROGEN	HEMATOCRIT	GENERAL	CLINICAL STATUS	TREATMENT
			m eq/l	m eq/l	m eq/l	m eq./l.	m eq./l.	gm/100cc.	mg/100cc.	mg./100cc.	%			
		Normal Values	150-155	139-141	4-5	1-7-5.4	102-106	6.4-7.5	1-1-5	20-35	40-45			
Pemphigus vulgaris acutus	I D	10/16/40	152	139	4.1	4.8	100	7.5	3.6	33	48	Good	0 (only oral)	Dihydrochaysterol started 10/16/40; adrenocortical extract started 10/25/40.
		12/1/40	140	130		5.3		5.8		38		Poor	++	
		12/7/40	156	142	3.8	8.1	101	6.1		80	27	Fair	+	
		1/31/41		131	3.9	7.1	95	6.0	1.6	71	22	Poor	++	
		3/19/41		145		5.6		6.0		37	16	Died	++	
R M		5/11/40	118	138	4.9	4.6	102	6.3		22	40	Fair	++	Vitamin D started 6/18/40.
		6/18/40		132		4.6	91	4.6		27	21	Poor	++	
		6/27/40		139		6.6			4.0	27		Fair	+	
		9/1/40	146	133		6.8				28	32	Died	++	
	H D	8/21/39	149	136	4.2	4.5	101	6.4	2.1	33		Fair	++	Dihydrochaysterol started 8/22/40; adrenocortical extract started 9/26/40.
N P		10/6/39	116	127		5.6		5.6	2.5	36	28	Poor	++	
		1/2/40		135	4.1	4.9	6.4	6.4		43	30	Fair	+	
		7/31/40		139		5.9		7.2	2.4	37	40	Well	0	
		10/11/40	151	133	5.1	4.5	103	6.3	4.2	32	39	Fair	+	Dihydrochaysterol started 10/15/40; adrenocortical extract started 11/6/40.
		10/19/40	141	129	5.1	4.3	91	5.5	1.1	31	38	Poor	++	
D F		10/27/40	141	134	4.1	5.6	92	5.4		39	32	Fair	+	
		12/16/40		129	4.6	5.3	93	5.3		51	38	Poor	++	
		1/11/41		119	4.5	6.0	116	5.0				Died	++	
		4/20/40	142	131	4.8	4.0	99	4.5	3.4	46	39	Poor	++	Adrenocortical extract started 4/20/40; vitamin D started 11/26/40.
		6/7/40	147	136	4.1	4.2	99	5.5	3.2	19		Fair	+	
F. S.		1/4/41		141		5.7		7.5		68		Good	(+)	
		3/12/40	151	141	4.4	4.3	106	5.3	2.0	26	41	Fair	++	Dihydrochaysterol started 5/25/40; changed to vitamin D 6/21/40.
		5/25/40	143	133	4.9	3.9	98	5.6	1.2	29	37	Poor	++	
		7/19/40		135		6.7		7.2		37		Fair	+	
		11/19/40		145	4.8	5.3		7.9		59	43	Well	0	Vitamin D started 6/5/40.
J. L.		6/5/40	148	137	4.2	4.1	106	6.2	2.7	19		Poor	++	
		7/2/40	153	141	3.2	7.3	108	7.2		26		Fair	+	
		7/30/40		141		7.3		8.0		28		Good	(+)	
		9/26/40	119	138	5.0	3.6	106	5.3	3.7	40		Poor	++	Dihydrochaysterol started 9/30/40; changed to vitamin D 11/1/40.
		1/7/41	154	145		6.3		5.9		58	18	Died	+	
D. P		6/20/40	147	136	4.5	4.6	101	6.0	2.1	38	14	Fair	++	Dihydrochaysterol started 7/19/40; adrenocortical extract given from 8/25 to 10/17; vitamin D instead of dihydrochaysterol after 11/13/40.
	A. J.	8/8/40		131		4.8	100	6.4		24	35	Poor	++	
		9/19/40		136	9.2	6.6		6.6		45	40	Fair	+	
		1/7/41	152	140		5.9		7.4		49	37	Well	0	
	I. W.	9/23/39		138		3.8	96	6.3				Fair	++	Vitamin D started 9/29/39.
	10/17/39	152	141	3.8	7.9		6.4	2.9		47	30	Good	+	

In 3 cases, there were small metastatic nodules in the gall bladder.

In 2 cases, the thyroid gland was implicated, each time by a metastasis secondary to tumor primary in the retroperitoneal nodes. In 2 cases, metastatic nodules were found in the testes.

There was involvement by the tumor of the following organs in 1 case each: ovary, uterus, iliac vein, bladder and dura.

SUMMARY

Hodgkin's paraganuloma, characterized by the presence of Reed-Sternberg cells in the absence of necrosis or fibrosis, appears to be a disease essentially of lymph nodes. With the passage of time, it may become transformed into the more malignant Hodgkin's granuloma.

Hodgkin's granuloma, characterized by the presence of Reed-Sternberg cells, pleomorphism, eosinophils, necrosis and fibrosis, may involve any organ of the body with the exception of the central nervous system proper and is frequently widespread.

Hodgkin's sarcoma, characterized by the presence of typical Reed-Sternberg cells scattered among cells that are probably extremely anaplastic forms of Reed-Sternberg cells, behaves as a true tumor, is highly invasive and malignant and may involve any organ of the body, including the central nervous system proper.

Transitional forms of these three types of Hodgkin's disease occur, but it is essential for the understanding of the clinical features to recognize the existence of each.

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PEMPHIGUS*

A Further Report on Chemical Studies of the Blood Serum and Treatment with Adrenocortical Extract, Dihydratachysterol or Vitamin D

WALTER F. LEVER, M.D.,† AND JOHN H. TALBOTT, M.D.‡

BOSTON

AS SHOWN in two recent communications,^{1,2} significant changes in the electrolyte content of the blood serum occur in patients with pemphigus vulgaris. In an attempt to correct the chemical changes, we have treated patients with pemphigus vulgaris with adrenocortical extract, dihydratachysterol or massive doses of vitamin D. In the first communication the results of treatment with adrenocortical extract in 5 patients with acute pemphigus were reported, and in the second the results of treatment with dihydratachysterol in 10 patients with chronic pemphigus.

From 1939 to 1941, 17 additional patients with pemphigus were studied and treated at the Mas-

sachusetts General Hospital. It is the purpose of this paper to report the chemical findings in the blood serum of these patients and to evaluate the effectiveness of adrenocortical extract, dihydratachysterol and massive doses of vitamin D in the treatment of this disease.

DIAGNOSIS AND PROGNOSIS

The various types of pemphigus differ not only in their clinical appearance and prognosis but also in regard to chemical changes and their response to treatment. It seems best to describe briefly the clinical appearance and the prognosis of each type before presenting the chemical data and therapeutic results. The quoted figures regarding the prognosis of the various types were obtained from a series of 62 patients with pemphigus admitted to the Massachusetts General Hospital between

*From the Dermatologic Clinic and Medical Clinic, Massachusetts General Hospital, and the Fatigue Laboratory, Harvard University

†Assistant, . . . Harvard Medical School, assistant in dermatology, . . . Hospital, junior associate in dermatology, Petri

‡Associate in medicine, Harvard Medical School, and assistant physician, Massachusetts General Hospital (on leave of absence)

pital began as pemphigus erythematosus. The mortality is zero in the localized type, but in cases in which pemphigus erythematosus develops into pemphigus foliaceus or vulgaris the prognosis changes accordingly.

Pemphigus Conjunctivae

Pemphigus conjunctivae (benign mucous membrane pemphigus) always attacks the mucous membranes and, in about half the cases, the skin. The conjunctivas are nearly always affected and occasionally represent the only area of involvement. The lesions always produce scarring of the conjunctivas, frequently scarring of other mucous membranes and occasionally scarring of the skin. Pemphigus conjunctivae is an extremely chronic affection but is benign in its course. It never causes a general feeling of illness and does not end fatally.

ELECTROLYTE CONTENT OF BLOOD SERUM

The present series of 17 patients includes 3 with pemphigus vulgaris acutus, 2 with pemphigus vegetans, 6 with pemphigus vulgaris chronicus, 4 with pemphigus foliaceus and 2 with pemphigus conjunctivae. The chemical data confirm the findings previously reported.^{1,2} Significant changes in the electrolyte content of the blood serum were observed in pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus. No consistent changes were noted in pemphigus foliaceus and pemphigus conjunctivae.

In patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus, the amount of sodium, chloride, calcium and protein in the blood serum was found to be reduced. Representative data of determinations at the time of admission and in the course of the disease are listed in Table 1. It is apparent that the degree of reduction usually corresponded to the severity of the clinical condition and to the amount of skin involved. In the earliest part of the disease, when only a few lesions were present, the chemical determinations usually showed normal values. For instance, patients I. D. and N. P., who at the time of admission showed only a few lesions, had normal values for nearly all constituents at that time. During the period of widespread cutaneous involvement the chemical changes were usually more pronounced in patients with pemphigus vulgaris acutus and pemphigus vegetans than in those with pemphigus vulgaris chronicus. The serum sodium was decreased in patients with pemphigus vulgaris acutus and pemphigus vegetans to values varying from 127 to 132 milliequiv. per liter, and in patients with pemphigus vulgaris chronicus to values varying from 131 to 138 milliequiv. per liter. The values for chloride closely paralleled those of the sodium. The protein was decreased to values varying from 4.6 to 5.8 gm. per 100 cc. in patients with pemphigus vulgaris acutus and pemphigus vegetans

and to 5.3 to 6.2 gm. in patients with pemphigus vulgaris chronicus. The decrease of serum calcium is less evident because most patients, soon after admission received dihydrotachysterol or massive doses of vitamin D, both of which produce a rise of the serum calcium within a short time. Nevertheless it is evident, even from the values obtained at the time of admission, that a decrease of the serum calcium is usually present in patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus.

In 4 patients with pemphigus foliaceus, chemical studies revealed no significant changes except that in 1 patient the serum protein was reduced to 4.3 gm. per 100 cc. None of the patients were, when studied, in the early bullous stage, but in the chronic exfoliative stage. It may be mentioned, however, that 1 patient of the previous series² who at the time of study had been in the early bullous stage had shown a reduction of the serum sodium to 136 milliequiv. per liter. Two patients with pemphigus conjunctivae showed normal values. Similarly, 1 patient with pemphigus erythematosus studied in the previous series² had shown a normal concentration of electrolytes in the blood serum.

TREATMENT WITH ADRENOCORTICAL EXTRACT, DIHYDROTACHYSTEROL AND VITAMIN D

Administration of adrenocortical extract produces an increase of sodium in the blood serum. This hormone has a sodium-retaining action, since it increases the reabsorption of sodium in the proximal segment of the renal tubules.¹⁴ Dihydrotachysterol, as well as vitamin D, produces a rise of the calcium content of the blood serum and subsequently an increased elimination of calcium through the kidneys. The rise of the serum calcium is accomplished by increased absorption of calcium from the intestinal tract and by resorption from the bones.¹⁵ A rise of the serum protein and serum sodium usually accompanies the rise of the calcium.¹⁶

The treatment with adrenocortical extract, dihydrotachysterol and vitamin D represents an attempt to correct the chemical changes observed in patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus. It was found that adrenocortical extract was the most effective drug in pemphigus vulgaris acutus and pemphigus vegetans, whereas dihydrotachysterol or massive doses of vitamin D produced the best results in pemphigus vulgaris chronicus. In several patients combined treatment with adrenocortical extract and dihydrotachysterol was used.

Adrenocortical extract was found in general to be superior to the synthetic preparation. The recommended dosage is 20 cc. a day for the first four days, and 5 to 10 cc. a day thereafter. Half the daily dose is injected intravenously and half intramuscularly. In addition, either an intravenous infusion of 1000 cc. of physiologic saline solution or 10 gm. of salt

1921 and 1936, none of whom received any of the treatments under discussion. A detailed clinical study of this group of patients has been published previously.³

There are three well-established types of pemphigus, namely, pemphigus vulgaris, pemphigus foliaceus and pemphigus vegetans. To these, two new types have been added in recent years — pemphigus conjunctivae or benign mucous-membrane pemphigus^{4, 5} and pemphigus erythematosis or Senear-Usher type of pemphigus.⁶ Furthermore, Brocq⁷ has suggested a division of pemphigus vulgaris into two types — an acute, malignant type (*pemphigus subaigu malin*) and a chronic, benign type. The septic (acute or butcher's) pemphigus, however, is no longer regarded as a disease entity. As stated elsewhere,⁸ it is believed that cases that in the past have been reported with this diagnosis can be classified as bullous impetigo, severe erythema multiforme or pemphigus vulgaris acutus.

Clinical study of the patients with pemphigus at the Massachusetts General Hospital has shown that separate consideration of these three additional types is justified.

Acute Pemphigus Vulgaris Acutus

Descriptions of pemphigus vulgaris acutus (*pemphigus subaigu malin* or malignant pemphigus vulgaris) have been given by Brocq,⁷ Lane and Lambert⁹ and Pelagatti.¹⁰ We^{11, 12} have discussed the clinical picture in two recent communications. The bullas are usually small and flaccid and break easily. Occasionally no bullas form on the skin and the epithelium merely slides off, leaving erosions, which tend to enlarge as the epithelium becomes detached at the periphery. By peripheral extension and confluence of the erosions large areas of the body may become denuded. The large erosions, which are the most important clinical sign of this type of pemphigus, show little tendency to heal. The oral mucosa is involved in nearly all cases. The mouth is frequently the site of the first lesions. The oral involvement, if present, is usually severe. Large denuded areas may develop in the mouth, just as on the skin, by peripheral extension of the erosions. In the severest stage almost the entire oral mucosa may be transformed into a single large, eroded surface. Frequently the lesions extend to the vermilion border of the lips, and hemorrhagic crusts form on the lips.

A large percentage of the patients are Jewish. The mortality among 22 patients seen at the Massachusetts General Hospital between 1921 and 1936 was 100 per cent. The average duration of the disease was seven and a half months.

Pemphigus Vegetans

As stated in a previous communication,¹¹ pemphigus vegetans resembles pemphigus vulgaris acutus in every respect except the vegetations

that form secondarily on the erosions. The prognosis is grave, although not quite so hopeless as that in acute pemphigus vulgaris. Fruhwald,¹³ in reviewing the outcome of 147 cases of pemphigus vegetans as reported in the literature, found the mortality to be 73 per cent. He believed, however, that some additional patients might have died subsequent to the time of publication.

Pemphigus Vulgaris Chronicus

In pemphigus vulgaris chronicus the bullas are usually tense and may attain considerable size, but do not break so easily as in the acute form of the disease. The erosions at the site of broken blisters do not extend to the periphery. The tendency of the erosions to heal is well pronounced. This form rarely starts in the mouth, and only about half the cases ever show involvement of the oral mucosa. The appearance of the oral lesions corresponds to that of the cutaneous lesions. One can frequently see intact blisters in the mouth, because they do not break easily. They are usually small, and the erosions at the site of broken blisters do not tend to increase in size, so that the oral involvement is never so extensive as in pemphigus vulgaris acutus.

Pemphigus vulgaris chronicus is apparently rare among Jews, since none of the patients with this form seen at the Massachusetts General Hospital since 1921 belonged to the Jewish race. The mortality in 16 patients seen between 1921 and 1936 was 50 per cent.

Pemphigus Foliaceus

Pemphigus foliaceus shows bullas only in the early stage and gradually assumes the appearance of a generalized exfoliative dermatitis, from which it is; however, easily differentiated by the presence of a positive Nikolsky sign. Oral lesions are absent. The mortality rate in the 14 patients with pemphigus foliaceus seen between 1921 and 1936 was 43 per cent. In those who survive, this disease may become extremely chronic. In 4 of the 14 patients who were first seen between 1921 and 1936, the disease has by now persisted for more than ten years. Age appears to be an important factor in the prognosis. In the patients who acquired pemphigus foliaceus before the age of thirty the mortality rate was 13 per cent; in those who acquired it at a later age it was 83 per cent.

Pemphigus Erythematosis

Many cases of pemphigus erythematosis (Senear-Usher type of pemphigus) may be regarded, as Gray¹⁴ has suggested, as a localized form of pemphigus foliaceus that may remain localized or change into pemphigus foliaceus. This concept cannot, however, be applied to all cases, since several reports have appeared in which pemphigus vulgaris subsequently developed. Three cases of pemphigus foliaceus seen at the Massachusetts General Hos-

pital began as pemphigus erythematosus. The mortality is zero in the localized type, but in cases in which pemphigus erythematosus develops into pemphigus foliaceus or vulgaris the prognosis changes accordingly.

Pemphigus Conjunctivae

Pemphigus conjunctivae (benign mucous membrane pemphigus) always attacks the mucous membranes and, in about half the cases, the skin. The conjunctivas are nearly always affected and occasionally represent the only area of involvement. The lesions always produce scarring of the conjunctivas, frequently scarring of other mucous membranes and occasionally scarring of the skin. Pemphigus conjunctivae is an extremely chronic affection but is benign in its course. It never causes a general feeling of illness and does not end fatally.

ELECTROLYTE CONTENT OF BLOOD SERUM

The present series of 17 patients includes 3 with pemphigus vulgaris acutus, 2 with pemphigus vegetans, 6 with pemphigus vulgaris chronicus, 4 with pemphigus foliaceus and 2 with pemphigus conjunctivae. The chemical data confirm the findings previously reported.^{1,2} Significant changes in the electrolyte content of the blood serum were observed in pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus. No consistent changes were noted in pemphigus foliaceus and pemphigus conjunctivae.

In patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus, the amount of sodium, chloride, calcium and protein in the blood serum was found to be reduced. Representative data of determinations at the time of admission and in the course of the disease are listed in Table 1. It is apparent that the degree of reduction usually corresponded to the severity of the clinical condition and to the amount of skin involved. In the earliest part of the disease, when only a few lesions were present, the chemical determinations usually showed normal values. For instance, patients I. D. and N. P., who at the time of admission showed only a few lesions, had normal values for nearly all constituents at that time. During the period of widespread cutaneous involvement the chemical changes were usually more pronounced in patients with pemphigus vulgaris acutus and pemphigus vegetans than in those with pemphigus vulgaris chronicus. The serum sodium was decreased in patients with pemphigus vulgaris acutus and pemphigus vegetans to values varying from 127 to 132 milliequiv. per liter, and in patients with pemphigus vulgaris chronicus to values varying from 131 to 138 milliequiv. per liter. The values for chloride closely paralleled those of the sodium. The protein was decreased to values varying from 4.6 to 5.8 gm. per 100 cc. in patients with pemphigus vulgaris acutus and pemphigus vegetans

and to 5.3 to 6.2 gm. in patients with pemphigus vulgaris chronicus. The decrease of serum calcium is less evident because most patients, soon after admission received dihydrotachysterol or massive doses of vitamin D, both of which produce a rise of the serum calcium within a short time. Nevertheless it is evident, even from the values obtained at the time of admission, that a decrease of the serum calcium is usually present in patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus.

In 4 patients with pemphigus foliaceus, chemical studies revealed no significant changes except that in 1 patient the serum protein was reduced to 4.3 gm. per 100 cc. None of the patients were, when studied, in the early bullous stage, but in the chronic exfoliative stage. It may be mentioned, however, that 1 patient of the previous series² who at the time of study had been in the early bullous stage had shown a reduction of the serum sodium to 136 milliequiv. per liter. Two patients with pemphigus conjunctivae showed normal values. Similarly, 1 patient with pemphigus erythematosus studied in the previous series² had shown a normal concentration of electrolytes in the blood serum.

TREATMENT WITH ADRENOCORTICAL EXTRACT, DIHYDROTACHYSTEROL AND VITAMIN D

Administration of adrenocortical extract produces an increase of sodium in the blood serum. This hormone has a sodium-retaining action, since it increases the reabsorption of sodium in the proximal segment of the renal tubules.¹⁴ Dihydrotachysterol, as well as vitamin D, produces a rise of the calcium content of the blood serum and subsequently an increased elimination of calcium through the kidneys. The rise of the serum calcium is accomplished by increased absorption of calcium from the intestinal tract and by resorption from the bones.¹⁵ A rise of the serum protein and serum sodium usually accompanies the rise of the calcium.¹⁶

The treatment with adrenocortical extract, dihydrotachysterol and vitamin D represents an attempt to correct the chemical changes observed in patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus. It was found that adrenocortical extract was the most effective drug in pemphigus vulgaris acutus and pemphigus vegetans, whereas dihydrotachysterol or massive doses of vitamin D produced the best results in pemphigus vulgaris chronicus. In several patients combined treatment with adrenocortical extract and dihydrotachysterol was used.

Adrenocortical extract was found in general to be superior to the synthetic preparation. The recommended dosage is 20 cc. a day for the first four days, and 5 to 10 cc. a day thereafter. Half the daily dose is injected intravenously and half intramuscularly. In addition, either an intravenous infusion of 1000 cc. of physiologic saline solution or 10 gm. of salt

in enteric-coated capsules is given daily. If the synthetic drug is used, the daily dosage recommended is 3 cc. intramuscularly during the first week, and 1 or 2 cc. thereafter. One thousand cubic centimeters of normal saline or 10 gm. of salt is also given daily. No toxic effects were observed as a result of this plan of treatment.

Dihydrotachysterol and vitamin D, which have a similar action on the calcium metabolism of the body, were found to possess the same degree of effectiveness. The optimal therapeutic effect was observed when the concentration of the serum calcium was raised above the normal level of 5 milliequiv. to a concentration of 6.5 to 7.5 milliequiv. per liter. This effect was usually accomplished by giving 10 or 15 cc. of dihydrotachysterol for seven to fourteen days. The serum calcium was maintained at this level in most cases by giving 3 to 5 cc. of dihydrotachysterol a day. Seventy-five thousand units of vitamin D was found to correspond approximately to 1 cc. of dihydrotachysterol in their calcium-raising effect. The two dangers of this treatment—namely, hypercalcemic coma with subsequent circulatory collapse and renal damage through mechanical obstruction of the tubules by calcium deposits—have been discussed in detail in the previous paper.² It had been stated that dihydrotachysterol and massive doses of vitamin D must be given with great circumspection to persons older than sixty and that it is contraindicated in patients with demonstrable renal insufficiency. Careful control of the level of calcium and non-protein nitrogen is required. These determinations should be carried out twice a week during the first few weeks and later once a week.

Administration of dihydrotachysterol or vitamin D in the recommended doses produced a rise of the calcium level above normal in all patients so treated (table 1). The rise usually began within one week. The effect of adrenocortical extract was less uniform. The rise of the sodium occurred often only after several weeks of treatment and, before the rise occurred, a continued decrease of the sodium was occasionally noted when the condition of the skin became worse.

Results

Treatment with adrenocortical extract, dihydrotachysterol or massive doses of vitamin D produced some favorable results in pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus, the three types of pemphigus in which a reduction of the serum sodium, chloride, calcium and protein occurs. The results of treatment in pemphigus foliaceus, pemphigus erythematous and pemphigus conjunctivae, in which no significant chemical changes are observed, were in general disappointing.

Fifteen case reports of patients treated with adrenocortical extract or dihydrotachysterol were

given in the two previous communications.^{1,2} For this reason, no case histories will be given here but the cases of each type will be discussed collectively.

Pemphigus vulgaris acutus. A total of 7 patients with pemphigus vulgaris acutus received treatment with adrenocortical extract, dihydrotachysterol or massive doses of vitamin D. Four of them died of pemphigus and 3 survived, a mortality of 57 per cent, compared with 100 per cent in 22 patients admitted between 1921 and 1936 who did not receive this treatment.

The course of 4 cases under treatment with adrenocortical extract was reported in detail in the previous communication.¹ Two patients died of pemphigus, one of them, however, only after he had a complete, although short, remission. Two patients were reported as cured. One of them is still living and well, and the other has since died from cerebral hemorrhages without having had any more lesions of pemphigus.

Between 1939 and 1941, 5 patients with pemphigus vulgaris acutus were treated. Two of them died after less than two weeks' treatment. These cases have been excluded from statistical consideration, because death occurred before treatment could have taken full effect. Of the remaining 3 patients, 2 died of pemphigus after a prolonged period of treatment and 1 is living. The 2 patients who died after prolonged treatment first seemed to respond to the treatment in that they had a complete remission lasting several weeks, but then relapsed in spite of continued treatment. The 1 living patient has been free from lesions for three years. The improvement that was observed in all 3 patients of the present series began three to six weeks following institution of treatment.

The question arises whether the observed remissions might not have been spontaneous. This is possible, but spontaneous complete remissions in pemphigus vulgaris acutus are rare and were, for instance, not observed in any of the 22 cases of pemphigus vulgaris acutus seen between 1921 and 1936. An incidence of 6 complete remissions in the 7 cases of both series seems significant.

Two of the 3 patients of the present series were treated with both adrenocortical extract and dihydrotachysterol or vitamin D and 1 with vitamin D alone. The surviving patient received both types of treatment. It seems that in acute pemphigus vulgaris it is advisable to use both types of treatment.

Pemphigus vegetans. Three patients with pemphigus vegetans were treated. Two of them died of pemphigus and 1 survived.

The course of 1 case treated with adrenocortical extract was reported in the previous communication.¹ The patient died after having had a complete remission lasting for five weeks.

The present series includes 2 patients with pemphigus vegetans. One died after having undergone

a complete remission lasting two weeks; the other is living. Improvement was observed in both patients approximately two to three weeks after treatment was begun. The surviving patient has had a few lesions in the anogenital region and in the oral cavity most of the time since her first discharge three years ago. On two occasions she had moderately severe relapses, which, however, subsided within a few weeks after resumption of treatment.

In spite of the fact that 2 of the 3 patients of both series finally succumbed, it appears significant that

no lesions of pemphigus present; the other 4 patients are living. The patient who died of pemphigus showed a satisfactory response so far as the cutaneous lesions were concerned, but had become extremely weak and anemic, death occurring when hypostatic bronchopneumonia developed. At the time of exitus only a few scattered, small bullas were present. Of the 4 living patients 3 are free from lesions and 1 occasionally develops a few lesions but is otherwise well. Two of the 3 patients who are free from lesions had a mild relapse after

TABLE 2. Results of Treatment with Adrenocortical Extract, Dihydratichysterol or Vitamin D.

TYPE OF DISEASE	NO OF PATIENTS	CURED	GREAT IMPROVEMENT	LITTLE OR NO IMPROVEMENT	DIED OF PEMPHIGUS	LIVING	DIED OF DISEASE OTHER THAN PEMPHIGUS
<i>Pemphigus vulgaris acutus</i>	7	3			4 (57%)	2	1
<i>Pemphigus vegetans</i>	3		1		2 (67%)	1	
<i>Pemphigus vulgaris chronicus</i>	14	11	1		2 (14%)	7	5
<i>Pemphigus foliaceus</i>	5		1	2	2 (40%)	3	
<i>Pemphigus erythematousus</i>	1		1			1	
<i>Pemphigus conjunctivae</i>	2			2		2	

all 3 patients showed complete remissions under treatment.

The surviving patient of the present series received treatment with adrenocortical extract, and the other received dihydratichysterol. It is believed that, just as in pemphigus vulgaris acutus, the combined treatment with adrenocortical extract and dihydratichysterol or vitamin D is advisable.

Pemphigus vulgaris chronicus. Fourteen patients with pemphigus vulgaris chronicus were treated.

treatment had been discontinued but recovered when treatment was resumed.

In 3 of the 6 patients improvement began within two weeks, in the other 3 patients after three to six weeks of treatment. Three of the 4 patients who showed complete healing were free from active lesions six weeks after treatment was begun, but 1 patient ceased forming lesions only after three months of treatment.

The treatment in 4 of the 6 cases of the present series consisted of dihydratichysterol in the begin-

TABLE 3. Comparison of the Mortality Rates of Patients Treated with Adrenocortical Extract, Dihydratichysterol or Vitamin D with Those of Patients Not So Treated.

TYPE OF DISEASE	PATIENTS SO TREATED			PATIENTS NOT SO TREATED		
	NO	DIED OF PEMPHIGUS	MORTALITY %	NO	DIED OF PEMPHIGUS	MORTALITY %
<i>Pemphigus vulgaris acutus</i>	7	4	57	22	22	100
<i>Pemphigus vegetans</i>	3	2	67	—	—	(73)
<i>Pemphigus vulgaris chronicus</i>	14	2	14	16	8	50
<i>Pemphigus foliaceus</i>	5	2	40	14	6	43
<i>Pemphigus erythematousus</i>	1	0	0	—	—	—
<i>Pemphigus conjunctivae</i>	2	0	0	10	0	0

Two of them died and 12 survived, a mortality of 14 per cent, compared with 50 per cent in the 16 patients not so treated.

Eight of the 10 patients reported previously² as having been treated with dihydratichysterol had pemphigus vulgaris chronicus. One of them was reported to have died from pemphigus, 4 as having died from other diseases with no lesions of pemphigus present, and 3 as living. These 3 patients are still living and well and have had no further treatment.

Six patients with pemphigus vulgaris chronicus were treated between 1939 and 1941. One died of pemphigus and 1 from cardiovascular disease with

ning and vitamin D later. In 1 of these patients adrenocortical extract was also given for seven weeks because of an extremely low serum sodium (131 milliequiv. per liter). Two patients received only vitamin D. Dihydratichysterol and vitamin D seemed to possess the same degree of effectiveness when given in corresponding doses.

Pemphigus foliaceus. The previous report concerning treatment of chronic pemphigus with dihydratichysterol² included 1 case of pemphigus foliaceus. This patient had come under treatment in the early stage of the disease when bullas were still present. The recovery under treatment with dihydratichysterol was slow but satisfactory. The

in enteric-coated capsules is given daily. If the synthetic drug is used, the daily dosage recommended is 3 cc. intramuscularly during the first week, and 1 or 2 cc. thereafter. One thousand cubic centimeters of normal saline or 10 gm. of salt is also given daily. No toxic effects were observed as a result of this plan of treatment.

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MEDICAL PROGRESS

DISEASES OF THE VEINS

JOHN HOMANS, M.D.*

BOSTON

VENOUS THROMBOSIS AND PULMONARY EMBOLISM

PATHOLOGISTS have long recognized the frequency of thrombosis in the deep veins of the lower legs. Only occasionally have impressive observations been reported; yet when post-mortem examinations have been made with the clinical problem in view, it has been discovered that following death from a great variety of causes, deep-venous thrombosis has been found below the knees in at least 25 per cent of all the subjects investigated. In some reports the percentage is much higher. A good example of a study of this sort, previously quoted in progress notes made by me in 1942, is that of Hunter, Sneed, Robertson and Snyder.¹ They undertook to discover the percentage of venous thrombosis of the lower leg in patients from a charity hospital, from a state psychopathic institution and from two private hospitals, believing, very naturally, that the background of the patient and the nature of his illness might influence the frequency of the disease. Needless to say, they were looking for the quiet type, — the so-called "phlebothrombosis" — which is necessarily little noticed clinically and that is recognized today as the usual source of pulmonary embolism.

They found thrombi of various ages to be present in 52.7 per cent of the 351 unselected middle-aged and elderly patients who had been forced to bed for varying periods before death. They studied microscopically 209 pairs of soleus and gastrocnemius muscles. Inasmuch as pulmonary embolism had been responsible for only 3.1 per cent of all the deaths in their series, it is evident that much of the thrombosis had either healed or was a terminal manifestation, not having advanced upward beyond the lower legs. This is in accordance with still earlier pathological observations of Rossle,² who found what may be described as terminal thrombosis in 25 per cent of all cases, and of Neumann,³ who reported isolated venous thrombosis confined to the

parts below the knees in 29 per cent of the bodies investigated. It appears that in the study of Hunter and his associates the percentage of lower-leg thrombosis in the various hospitals was 59 per cent in the charity hospital, 49 per cent in the state psychopathic institution and 40 to 42 per cent in the two private hospitals. From such figures as these one is justified in concluding that confinement to bed, whatever its cause, tends to lead to thrombosis in the veins of the legs and that the more enfeebled patients show a higher percentage of disease than do the better preserved ones. Indeed, it has been too little recognized that serious illnesses, including those of the heart itself, are frequently complicated by quiet thrombosis and fairly often terminated by pulmonary embolism. Rossle,² in the study of his relatively small series, remarks that the death of the patient cuts off the development of many low processes that would otherwise have spread upward into the femoral vein. One need not follow this line further, but need only recognize that here is a background against which observations made during life may be interpreted.

An important aspect of deep venous thrombosis is the causal relation of trauma, in the broad sense. One must think of surgical operations — unfortunately — in this connection, especially in patients suffering from cancer or other debilitating diseases, but fracture of any bone of the lower limbs, including those of the feet, whatever the form of fixation used, must be regarded as almost as important a cause of thrombosis and pulmonary embolism. My⁴ first experiences with actual or threatened embolism arose from metatarsal fractures in vigorous middle-aged persons. Just where post-partum thrombosis belongs in the picture is difficult to say. There is reason, of course, to suspect an entirely pelvic origin, but since there is nothing about a "milk leg" that is essentially different from any other thrombophlebitis, the lower leg should, for the moment, be regarded as its chief source.

How does such thrombosis arise? Wright^{5, 6} offers a reasonable explanation for what may be at least

*Clinical professor of surgery, Tufts College Medical School, clinical professor of surgery, emeritus, Harvard Medical School, consultant in surgery, Peter Bent Brigham Hospital and Joseph H. Pratt Diagnostic Hospital

patient has had occasionally during the last four years a few erythematous lesions on the skin, but the Nikolsky sign has been negative and he has been able to do heavy labor.

Four more patients with pemphigus foliaceus were treated between 1939 and 1941. All came under treatment at a time when bullas were no longer present. They presented the appearance of a generalized exfoliative dermatitis. All of them were treated with either dihydrotachysterol or massive doses of vitamin D. None of them showed improvement. Two died and 2 are living.

Pemphigus erythematosis. One case of pemphigus erythematosis treated with dihydrotachysterol was included in the previous report.² The patient had shown slow improvement. At present the patient still has a few scattered lesions.

Pemphigus conjunctivae. Two patients with pemphigus conjunctivae were treated for an extended period with massive doses of vitamin D. Both had conjunctival and oral lesions. No improvement was noted in either case.

DISCUSSION

No etiologic significance can be attached to the chemical changes observed in pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus. In the first place, during the earliest part of the disease when there were only a few lesions present the chemical determinations usually showed normal values. Furthermore, 3 of the 4 patients who died of pemphigus had at the time of death abnormally high sodium concentrations and 3 had abnormally high calcium concentrations in the blood serum. Although the high values can be attributed to the treatment, the fact that they were encountered at the time of death excludes sodium or calcium deficiency as a primary factor in the cause of the disease. The reduction of the serum sodium, chloride, calcium and protein is therefore regarded as a secondary symptom produced by the disease. It is possible that the chemical changes are due to the loss of plasma through the cutaneous lesions and the resulting osmotic changes. Damage to the adrenal glands, as observed in 2 patients with pemphigus vulgaris acutus and reported in one of the previous communications,¹ may be a factor of importance in some cases.

The favorable results obtained by treatment with adrenocortical extract, dihydrotachysterol or massive doses of vitamin D in some cases of pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus are apparently based on the tendency of these drugs to correct the chemical changes that occur in these forms of pemphigus. Since the chemical changes are secondary symptoms produced by the disease, the treatment is regarded as merely symptomatic. Although its limitations are fully realized, it is believed that it may well be

tried in patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus, not only as a measure for correction but also as a means for prevention of the chemical changes. Whether or not treatment with dihydrotachysterol or massive doses of vitamin D is of any value in the early, bullous stage of pemphigus foliaceus is a question that only further investigation can decide.

SUMMARY

Six types of pemphigus are recognized — pemphigus vulgaris acutus (Brocq's *pemphigus subaigu malin*), pemphigus vegetans, pemphigus vulgaris chronicus, pemphigus foliaceus, pemphigus erythematosis (Senear-Usher type of pemphigus) and pemphigus conjunctivae.

In pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus, the amount of sodium, chloride, calcium and protein in the blood serum was found to be reduced. These changes were more pronounced in pemphigus vulgaris acutus and pemphigus vegetans than in pemphigus vulgaris chronicus. The degree of reduction usually corresponded to the severity of the clinical condition and the amount of skin involved.

No etiologic significance can be attached to the chemical changes. They are regarded as a secondary symptom produced by the disease.

Thirty-two patients with pemphigus were treated with adrenocortical extract, dihydrotachysterol or massive doses of vitamin D. Encouraging results were obtained in several patients with pemphigus vulgaris acutus, pemphigus vegetans and pemphigus vulgaris chronicus. The results of treatment in patients with pemphigus foliaceus, pemphigus erythematosis and pemphigus conjunctivae were in general disappointing.

The treatment tends to correct the reduction of sodium, chloride, calcium and protein encountered in such patients. Since it is believed that the chemical changes are secondary symptoms produced by the disease, the treatment is merely symptomatic.

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ferently. Welch and Faxon⁹ seem to think that since the diseases merge into one another, the distinction between them is not of fundamental importance. All agree, however, that from the solid, inflammatory thrombus, pulmonary emboli are very unlikely to be detached, whereas with the quiet, nonobstructive one, much more like a soft clot, embolism is always threatened. Ochsner and DeBaKey point out the wisdom of relaxing the various sorts of vasoconstriction in thrombophlebitis by a lumbar sympathetic block, and what may be called "the Boston school," including Welch and Faxon,⁹ Welch, Faxon and McGahey,¹⁴ Allen, Linton and Donaldson,¹⁵ Fine and Sears,¹⁶ Fine, Frank and Starr,¹⁷ myself and others, has long advocated, for the quiet phlebothrombosis, division of the principal vein of the limb or limbs affected, with the idea of halting the process and of preventing pulmonary embolism. Hence the importance of distinguishing between the two types — or, it may be, stages — is obvious.

DIAGNOSIS

In their recent paper, Allen, Linton and Donaldson¹⁵ make the point that if one could see a four-hourly temperature chart of every patient subject to the possibility of venous thrombosis in the legs, there would be evident, as the earliest sign of embolic detachment, a rise of pulse rate and temperature. I myself believe that entirely apart from gross embolism, a soft propagating thrombus often gives off small fragments that, without causing outspoken signs, disturb the pulmonary circulation, causing an increased respiratory and cardiac rate. One notices, for instance, after effective interruption of the principal vein or veins proximal to the thrombus, an immediate easing of the clinical situation, much more definite than might come, for example, through relief of the patient's anxiety, if such were present. Thrombosis itself need occasion no rise whatever, and there is often an interval of hours or days between the rise and the first thoracic symptoms of gross embolism. The trouble with this observation is that it is usually made in retrospect, and of course there are other causes of an elevation in the pulse rate and temperature curve besides the onset of embolism. Observation of the chart should be regarded as of the very first importance, however, and, along with the various physical signs in the legs themselves, is extraordinarily helpful. DeTakats¹⁸ takes this view, saying that a slight rise of temperature and a persistently elevated pulse rate, without apparent cause, after the fourth or fifth post-operative day should make one seek other signs of latent thrombosis. Among other things, he is interested in the skin temperature and soreness to touch of the sole of the foot. Allen and his associates¹⁵ mention in the order of their frequency a number of positive findings. In their series, some degree of swelling was found in 67 per cent of the

237 cases examined, tenderness was found in 61 per cent of 231 cases investigated with that finding in view, and in 139 cases examined for what they called "Homans's sign," — I prefer to call it the dorsiflexion sign, — this was found to be present in 42 per cent. I regard this dorsiflexion sign as having a greater degree of importance than would be judged from this analysis. Actually, dorsiflexion of the feet is intended to bring out, on the side of the venous thrombosis, some degree of irritability of the posterior muscles, the soleus and gastrocnemius. Discomfort need have no part in this reaction. Dorsiflexion may be less complete in response to an equal degree of upward pressure on the affected side as compared with the normal, or the patient may involuntarily flex the knee as the forefoot is forced upward, to release the tension on the posterior muscles. If one looks on the dorsiflexion sign as evidence of even the faintest irritability of the posterior muscles, — the early stage of the thrombosis occurring within and about them, — the sign will probably be found present more frequently than either tenderness or swelling.

Pulmonary embolism. As Allen and his associates note, pulmonary embolism is the first evidence of deep venous thrombosis in the lower limbs in a considerable proportion of cases — 41 per cent in their series. This does not mean that signs in the legs may not have been present but that none have been observed. It is true, however, that in a surprising number of persons some sort of thoracic distress or pain, or breathlessness, or cough gives the only hint that a quiet thrombosis in the legs is going on. This is in accordance with the general rule recognized by all those familiar with this subject; namely, that the more silent and less inflammatory the thrombosis in the lower limbs, the likelier is the process to cause pulmonary embolism. An outspoken thrombophlebitis, being an adherent, occluding process, rarely occasions any such accident. The quietest sort of thrombosis may occupy only a small stretch of vein among the calf muscles yet give rise to a long, hanging, potentially fatal thrombus.

Although it is not properly a subject of these notes, attention is called here to the importance of the electrocardiogram in the diagnosis of pulmonary embolism. As early as 1935, McGinn and White¹⁹ described cor pulmonale and its characteristic physical and electrocardiographic signs. In a recent communication, Murnaghan, McGinn and White²⁰ develop further the whole subject of the electrocardiographic diagnosis of pulmonary embolism, citing a number of clinical reports. Among their series of 10 cases were 3 of pulmonary embolism following bone injuries in women over sixty, 3 of postoperative embolism, 2 of these occurring in the third decade, and 3 in which the patients presented pulmonary symptoms from the beginning of their illness. Nine of these 10 patients had two or more attacks of infarction, the tenth only one. In 3 cases,

a contributing factor. He finds that the blood-platelet count rises following childbirth and surgical operations. The rise begins on the fourth day and reaches its maximum on the twelfth, falling back to normal on the twenty-first. There is a rough correspondence here with the clinical onset of thrombosis. But platelets do more than multiply. According to Wright, they become "sticky." Adhesiveness increases as the thrombocytes grow in number and is attributed to the quality of the platelets rather than to a change in the serum. Such phenomena have not been invoked in explanation of nontraumatic forms of venous thrombosis; that is, those that so frequently complicate serious illness, as well as the less common ones of active life. They may not perhaps be of great significance and they are certainly not fundamental. Even if invoked to explain postoperative thrombosis, they can hardly apply before the fourth day; and Newburger,^{7*} in a recent collective review of early postoperative walking, notes that since those physicians who got their patients out of bed on the third day still encountered thrombosis and embolism, thrombosis must often begin earlier—a suggestion in which I concur. Probably the moment of onset varies considerably and one must continue to regard life in bed, the reclining position, abdominal distention, enfeeblement of the circulation and elevation of venous pressure in the lower limbs, perhaps combined with muscular relaxation and atrophy of the legs, as of first importance.

A recent development, stimulated by White's⁸ observations on patients suffering from, or thought to be suffering from, cardiac or pulmonary disease, is the realization that quiet thrombosis may take place not only in persons already incapacitated by a cardiac disorder of some sort but in others apparently leading an active and sufficiently normal life. Such persons may even be young,—that is, in their teens,—although pulmonary embolism in the first four or five decades is unusual. That fatal embolism seldom occurs before the age of fifty was brought out by Welch and Faxon⁹ in their study of patients, mainly postoperative, at the Massachusetts General Hospital in 1941. I myself,¹⁰ dealing with a necessarily small ambulatory group, some of whom, because of repeated nonfatal embolism, had been falsely accused of suffering from angina or disease of their coronary arteries, have found the same thing to be true. Quiet venous thrombosis in the deep veins of the lower legs may take place at any age, although increasing in frequency with the years, but a fatal accident before the fiftieth year is rare. It is remarkable how often pulmonary embolism may occur and recur in ambulatory patients and how likely such persons are to be suspected of cardiac or pulmonary ailments rather than of

embolism from an unnoticed deep thrombosis in the lower legs. It is not even necessary that the patient should have suffered from an old thrombophlebitis now canalized. The veins of the legs may previously have been, so far as one can learn, entirely normal, giving no excuse whatever for a thrombotic process. As will appear later, the patient of fifty or over who suffers from an arterial deficiency is probably more liable to venous thrombosis, and perhaps embolism as well, than is the normal person. The thrombosis of active life does not, of course, crop up nearly so often as that of post-operative, post-traumatic and post-partum states, to say nothing of generalized circulatory failure, but is brought up here because physicians and laity alike are only too apt to deny the possibility of its occurrence.

COURSE OF LOWER-LEG VENOUS THROMBOSIS

In the recent paper to which allusion has just been made¹⁰ and in a paper presently to be published,¹¹ I call attention to the various courses that may be pursued by a venous thrombosis beginning in the lower leg or foot. I point out that the process may remain local without causing pulmonary embolism, that it may form a dangerous propagating thrombus that spreads up into the femoral vein and is the usual cause of the most serious sort of embolism, that it may extend upward in a more or less adherent form, partly filling the femoral and iliac veins, a rather prolonged disease with which a complicating thrombosis of the deep muscular veins of the thigh is likely to be associated, and which often ends fatally or that it may extend upward in a quiet form until, for reasons of which nothing is as yet known, it acquires an inflammatory element, to plug completely the femoral and iliac veins, causing swelling of the entire leg and the familiar picture of phlegmasia alba dolens. In this fourth course, the commonest, perhaps, in past experience, a non-suppurative infection appears to be the added feature, leading to perivascular involvement that affects the arterial wall as well as the various sorts of nerves surrounding the great vessels in the region of the groin and pelvis. As a result of this perivascular inflammation, there occurs not only some degree of local contraction of the companion artery but by what seems to be a reflex mechanism, a generalized constriction of the vessels of the entire limb. This condition has been called "thrombophlebitis" in contradistinction to the quiet disease or, if one likes, the quiet preliminary stage of this same process, dubbed by Ochsner and DeBaKey¹² "phlebotrombosis."

Various opinions have been expressed concerning the importance of a distinction between phlebotrombosis and thrombophlebitis. In a recent paper, Ochsner and DeBaKey¹³ make no attempt to trace the connection between them, but dwell very properly on the necessity of treating the two sorts dif-

*The review, by the way, shows that early postoperative walking is of advantage in more ways than one. Even if it does not do away with postoperative thrombosis and embolism, it appears to diminish its incidence rather than otherwise.

heparin for the most part intramuscularly. They find that in the "coumarinized" patient, the effect of a single intravenous injection of heparin is to sustain a prolonged clotting time for even as long as twenty-four hours. Thus heparin need not be given continuously, and intramuscular doses* can be substituted. Following an initial pulmonary embolism, they give heparin intravenously for a few hours. In the meantime, dicoumarol is started by mouth and, after the intravenous heparin has taken effect, intramuscular injection of the drug is begun. They indicate that two 5-cc. doses of heparin each day are sufficient. Three hundred milligrams of dicoumarol is given by mouth the first day, 200 mg. the second, and thereafter the dosage is governed by the prothrombin level. To use this system safely, prothrombin levels must be determined daily and the clotting time measured twice daily, clearly a matter requiring adequate and intelligent assistance, by no means foolproof. Their observations have been made experimentally and on a series of 15 patients without accident.

Barker, Allen and Waugh,³² from the Mayo Clinic, treated a series of 497 cases, all postoperative. Their principal groups included those who had already survived a pulmonary embolism and those who had had postoperative "thrombophlebitis." They used dicoumarol principally. They made no attempt to distinguish phlebothrombosis from thrombophlebitis. They do not state how long their patients were followed (to detect late embolism after withdrawal of the drug). They had 47 cases — 10 per cent — of more or less serious bleeding and 1 fatal hemorrhage. Nevertheless they believe that they reduced embolism far below expectation according to the system of statistics used, and conclude:

Adequate elevation of prothrombin time by means of administration of dicoumarol by mouth to postoperative patients is apparently effective in preventing postoperative thrombosis and pulmonary embolism. A plan of administration whereby 300 mg. are given on the first day, 200 mg. on the second day and 200 mg. on each subsequent day that the prothrombin time is less than thirty-five seconds (normal, eighteen to twenty-two seconds) has proved satisfactory. At present it is unwise to give dicoumarol unless the prothrombin time can be determined accurately each day. There is some risk of bleeding in postoperative cases when dicoumarol is given, but this risk is comparatively small. If hemorrhage occurs, it can be controlled by transfusion of freshly drawn blood.

In an editorial, DeBakey³³ expresses the opinion that at the present time the postoperative use of anticoagulants is too apt to cause hemorrhage and that proximal ligation of the thrombosed vein is to be preferred. He voices distrust of the type of

statistics employed by Barker and his associates. I believe, however, that it would not be at all surprising if the combined administration of heparin and dicoumarol should prove exceedingly helpful when all known safeguards are used, and especially if discrimination is exercised in the selection of cases. DeTakats³⁴ has put forward a test for heparin tolerance, that is, the reaction of the patient's coagulation time to a standard intravenous dose of heparin. He finds that some patients are resistant to heparin; that is, they are thrombophilic, especially in the early postoperative period, following cardiovascular accidents and in Buerger's disease. Others are heparin-sensitive. His observations on various methods of giving heparin should be studied, and he recommends frequent tests, by the capillary glass-tube method, of the coagulation time. He advocates the combined use of heparin and dicoumarol.

Surgical treatment. Section or ligation of veins as a means of therapy seems to have been advocated chiefly by Boston surgeons. The recent publication of Allen, Linton and Donaldson¹⁰ gives as fair a picture of indications and results as is at present available. The tendency is to use exploration of the superficial or common femoral vein for all early cases in which quiet thrombosis has been diagnosed, whether or not embolism has occurred, and to suck the thrombus out of the vein proximal to the groin whenever it is encountered. Allen and his associates, although constantly trying to improve their "diagnostic acumen," believe that in their attempt to cut off all possible sources of pulmonary embolism they will inevitably perform some unnecessary operations. I¹⁰ have employed similar methods but have attempted to distinguish the more chronic and recurrent forms of thrombosis marked by extension of the quiet process into the iliac veins. For such cases I have employed section of the common iliac vein, which I advocate, and in a paper now in publication I¹¹ debate the pros and cons of this higher operation and the indication for ligation of the lower vena cava, a procedure that surely has a limited though definite field of usefulness. In this connection, it is of considerable interest that Shackelford and Whitehill³⁵ report the successful section of the left common iliac vein in a soldier, twenty-eight years of age, who had suffered repeated pulmonary embolism during active military service. The patient had malaria, but the connection of the disease with venous thrombosis in the lower limb was probably not important.

For the technic of the various operative procedures to be employed one may consult the writings of Welch and Faxon,⁹ Welch, Faxon and McGahey,¹⁴ Allen, Linton and Donaldson,¹⁵ Fine and Sears,¹⁶ Homans³⁶ and others, but there are problems as yet unsolved. For example, if one is making an exploration of the vessel at the groin and finds a palpably thrombosed but presumably not fully ob-

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the electrocardiogram gave the first suggestive laboratory evidence of the correct diagnosis; in the rest it confirmed a clinical diagnosis. From the Mayo Clinic comes another report by Currens²¹ dealing with the importance of the electrocardiogram in the diagnosis of pulmonary embolism. This observer holds that the strain on the right ventricle seems to be the dominant factor in causing the electrocardiographic changes.

Phlebography. This diagnostic aid has proved, on the whole, disappointing. It has been advocated as a trustworthy means of making an early diagnosis (following the lead of dos Santos²² and of Bauer²³) by Welch, Faxon and McGahey,¹⁴ by Starr, Frank and Fine²⁴ and, more recently, by DeBakey, Schroeder and Ochsner.²⁵ On the other hand, Allen, Linton and Donaldson,¹⁵ reversing the opinion expressed earlier by the Massachusetts General Hospital group, find it rather untrustworthy, for, as they say, phlebograms are difficult to interpret and may be misleading. In this latter view, I join. The phlebogram, if positive, is sometimes astonishingly accurate and defines the thrombus and its extent in a way that no other diagnostic procedure can do, but in too many cases it leaves the diagnosis unproved, particularly in cases in which it is imperative that further pulmonary embolism should be prevented, and sometimes it suggests a positive diagnosis of thrombosis when no such process is present. In other words, the filling of the deep veins of the lower leg by a solution opaque to the x-ray is a somewhat uncertain procedure. I have found it most useful and reliable in giving information concerning a past or present thrombosis in the femoral vein, that is, in the deep vein above the knee. In the case of a rather chronic process, it may be very helpful to know whether to section the femoral vein proximal to the thrombus or whether one must go higher and expose the common iliac or the vena cava, but this is by no means making a diagnosis in the early or doubtful case; it is merely a refinement of a diagnosis already made.

TREATMENT

Heparin and dicoumarol. When one reads the publications of those accustomed to deal with deep venous thrombosis and pulmonary embolism by operative means, one is hardly made aware that such a treatment as the administration of heparin or dicoumarol exists. Yet when one reads Murray's²⁶ statement that, following an initial pulmonary infarction, not one of his 46 heparinized patients suffered a fatal pulmonary embolism, one must agree that there is virtue in this method. A recent report by Evans,²⁷ from the Lahey Clinic, on a short series of cases in which he depended mainly on dicoumarol (with which he sometimes combined heparin) presents certain advantages for this line of treatment, although it must be admitted that the death of 2

patients in 56* from hemorrhage is disconcerting, to say the least. So far as Boston is concerned, Evans appears to be a voice crying in the wilderness, but he receives support from other parts of the country. A recent editorial in the *Journal of the American Medical Association*²⁸ comments favorably regarding the prevention of venous thrombosis by the administration of dicoumarol to the experimental animal.

What troubles me in attempting to assay the value of the heparin-dicoumarol treatment is that in the reports I have so far studied, *postoperative* thrombosis has been, practically speaking, the only sort on which a trial has been made, thrombophlebitis has been lumped together with the quiet, dangerous type, — 13 out of Evans's 17 postoperative cases were of the inflammatory, obstructive sort, whereas only 4 represented phlebothrombosis — and, moreover, no parallel series of operative versus drug therapy in any large clinic is known to me to have been undertaken. Actually, the great field of thrombosis and embolism in those confined to bed by cardiac, pulmonary and other serious diseases has hardly been touched. These are fundamental omissions. It only appears, so far, that heparin is capable, if properly administered, of preventing the onset of thrombosis; that is, if given after operation, thrombosis and embolism are unlikely to occur. This, of course, is good, and if heparin were not so expensive and its administration were not so difficult and time-consuming a matter, heparinization, as a prophylactic, at least, could be freely recommended. So far as heparin alone is concerned, one cannot go much farther. Many surgeons believe that if given carefully, when pulmonary embolism has already taken place, it will halt embolism during the actual period of its administration but will not prevent a fatal recurrence following withdrawal of the drug.

Dicoumarol, in contrast with heparin, is cheap, is given by mouth and, by profoundly lowering the prothrombin level in the blood, prevents thrombosis. Thus it has certain advantages. But whereas heparin acts to prevent both clotting and adhesiveness of the thrombocyte (a basic part of thrombosis) only during its administration, and rapidly leaves the blood stream as soon as no more is introduced, dicoumarol continues to hold down the prothrombin level for many days after even moderate doses. Yet it does not delay coagulation. It may even cause serious or fatal bleeding while not prolonging the clotting time at all, and its dangerous effect can only be combated by the introduction of prothrombin through abundant transfusion of whole blood. For such reasons, Rhoads, Walker and Panzer²⁹ believe that dicoumarol and heparin should be looked on as complementary drugs and should be given together — dicoumarol by mouth and

*Actually only 46 cases of thrombosis or with a history of venous thrombosis were treated with dicoumarol and no deaths from hemorrhage occurred among them

heparin for the most part intramuscularly. They find that in the "coumarinized" patient, the effect of a single intravenous injection of heparin is to sustain a prolonged clotting time for even as long as twenty-four hours. Thus heparin need not be given continuously, and intramuscular doses* can be substituted. Following an initial pulmonary embolism, they give heparin intravenously for a few hours. In the meantime, dicoumarol is started by mouth and, after the intravenous heparin has taken effect, intramuscular injection of the drug is begun. They indicate that two 5-cc. doses of heparin each day are sufficient. Three hundred milligrams of dicoumarol is given by mouth the first day, 200 mg. the second, and thereafter the dosage is governed by the prothrombin level. To use this system safely, prothrombin levels must be determined daily and the clotting time measured twice daily, clearly a matter requiring adequate and intelligent assistance, by no means foolproof. Their observations have been made experimentally and on a series of 15 patients without accident.

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*Very likely further satisfactory intramuscular or subcutaneous means of administering heparin will be developed. Recently a method has been reported from the Mayo Clinic by Bryson and Code,³⁷ who administered subcutaneously a suspension of powdered heparin in a beeswax-stearine oil mixture and found that a satisfactory and prolonged coagulation time could be secured in the experimental animal. The method has been tried out on several patients. Bryson and Code allude to previous observations of Loewer, Rosenblatt and Lederer,³⁸ who gave heparin in a mixture of gelatin, acetic acid, glucose, a vasoconstrictor drug and water, reporting satisfactory observations on rabbits. It will be interesting to hear further from such attempts, which sound decidedly promising.

structed femoral vein, is it better to suck out all removable thrombus and section the vein, or shall one leave the vein alone and, closing the wound, undertake a common iliac division or even ligation of the vena cava? This matter is urgent because one may fail to remove all thrombus by suction, and subsequently, further detachment of material from some part of the iliac veins may occur. Another problem is the question whether, in such a case as has just been postulated, heparinization or a combined administration of heparin and dicoumarol shall follow the operation. Still another uncertainty is whether bilateral femoral division shall be performed in all cases of serious pulmonary embolism even though only one limb clearly exhibits signs of thrombosis. Finally, in the case of a breathless patient whose pulmonary arteries are evidently full of emboli and whose lower limbs show no convincing signs of thrombosis, shall one undertake the risk of attempting a division of the vena cava, or shall one expose both femoral vessels and suck out the soft thrombus, or shall one abandon operative surgery altogether and attempt to cure the patient by the combined use of heparin and dicoumarol? Settlement of these matters is most urgent in the case of extremely ill medical patients, especially those suffering from cardiac disease, for which a wide-awake medical service in any large hospital is likely in these days to seek treatment. Embolism may already have occurred without any positive signs of thrombosis in the legs, or in the absence of any signs of embolism, the legs themselves may be suspected of harboring a deep thrombosis. In a two-month period (February and March, 1944) at the Peter Bent Brigham Hospital, twelve vein interruptions were performed on medical cases as compared with six surgical ones. Most were femoral sections, but two ligations of the vena cava were made. The higher operations are most decisive, but are they too dangerous? If a general anesthetic seems to carry too great a risk, division of the vena cava can perhaps be performed under a right-sided paravertebral procaine block. Doubtless, the patient's economic situation, the operator's skill and the familiarity of all concerned with the various methods of treatment will be found to be controlling factors in standardizing treatment.

Ligation of the vena cava has long been practiced sporadically by gynecologists and obstetricians. A recent account has been given by Collins, Jones and Nelson.³⁷ Of course, the thromboses beginning in the pelvis, and especially those of a septic sort following uterine infection, require section of the ovarian veins as well as of the vena cava itself and therefore call for a transperitoneal operation. It appears that such a procedure is somewhat different in its effect from division of the vena cava alone in the case of thrombosis beginning in the legs, and the results of the operations performed because of thrombosis complicating pelvic sepsis

should not be used as guides in interpreting the after-effect of extraperitoneal ligations of the vena cava for phlebothrombosis of the lower leg. Undoubtedly my experience with section or ligation of the common iliac vein indicates that the venous return from the lower limb following this operation is much more satisfactory than that following division of the femoral vein. The same is not quite true of division of the lower vena cava, for in that case shunting of the blood from one side of the pelvis to the other is not available. It is proper to say, however, that in the observation of the dozen or so cases of division of the vena cava of which I have knowledge (unpublished observations), the subsequent venous return from the legs has been remarkably satisfactory and no serious aftereffects have as yet been observed.

It will be noted that nothing has been said of the treatment of thrombophlebitis (phlegmasia alba dolens) by lumbar sympathetic procaine block. Actually no new information as the results of this valuable procedure has appeared within the last two years.

VENOUS THROMBOSIS ASSOCIATED WITH ARTERIAL OBSTRUCTION

The association of venous thrombosis with arterial obstruction of various sorts, particularly in the lower limbs, has received insufficient attention. It would be rather trite to observe that there is such a disease as thromboangiitis obliterans, a disease in which venous and arterial thromboses are intimately associated. It is not even known, for instance, whether the primary process lies in one sort of vessel or the other. One sees, however, occasional cases in which arterial stoppage is obviously primary, yet with which there is so much venous stasis as to suggest that venous has become associated with arterial obstruction. I have also encountered pulmonary embolism in combination with some rather chronic arterial deficiencies. In this connection, an unusual paper was published some years ago by Cornil, Mosinger and Audier.³⁸ After calling attention to the association of phlebitis with arteritis in Buerger's disease and pointing out that arterial symptoms are frequently present with thrombophlebitis, they undertake to explain how thrombosis may be communicated from large artery to companion vein or from companion vein to large artery. They believe that with perhaps 40 per cent of arterial closures there is an associated venous thrombosis. In explanation, they show that the media and adventitia of the veins contain capillary vessels, supposedly lymphatic, which they find present only in the adventitia of the arteries. An inflammatory reaction starting within the arterio-venous sheath may extend, therefore, in a lateral direction and even longitudinally, the subsequent lateral extension producing results at a distance from the original lesion. When an inflammation

reaches the vein from the artery, it may occupy both the adventitia and the media, a phenomenon that would explain the frequent thrombosis of large veins associated with arterial disease. But when an inflammatory process is communicated from vein to artery, it involves only the adventitia and so causes spasm of the arterial wall rather than thrombosis. All such reactions depend on the enclosure of large arteries and veins in a common sheath within which are included the anastomosing lymphatic vessels.

Several communications are available relating to the presence of venous thrombosis and even pulmonary embolism in obstructive arterial disease. Veal³⁹ finds it worth while, in thigh amputations for gangrene of arterial origin, to ligate the femoral vein before amputation is performed. He believes that by so doing he prevents considerable pulmonary embolism. Atlas⁴⁰ describes a rather complicated case of thrombosis and embolism following amputation in which he was obligated to divide the vena cava, and I (unpublished data) have noticed, in connection with an unexplained arterial embolism that had caused gangrene of the lower leg, an associated thrombosis of the femoral vein obviously secondary to the lodgment of the embolus. This was discovered in an exploration of the femoral vessels at the groin in a search for the cause of the gangrene. Resection of that part of the artery containing the embolus, and of the companion vein as well, was employed. Such observations as these offer an explanation of the obvious venous engorgement associated with some fairly acute and outspoken obstructions in the femoral artery and perhaps account for the heat that is present in the feet of some of these patients, a heat obviously not due to infection and rather difficult to explain solely on a basis of a sudden cutting down of the arterial stream. Possibly, venous thrombosis associated with a sudden arterial occlusion is a useful natural provision, raising the venous pressure in the periphery of the limb and so actually improving the nutrition of the peripheral parts. Occasionally, of course, the associated venous thrombosis is a quiet one, almost necessarily overshadowed by the arterial occlusion, and if only partly obstructive is of the type that causes pulmonary embolism.

Venous pressure and the arterial circulation. Although not strictly relevant to the subject of diseases of the veins, the reaction of local venous pressure in a limb on the arterial circulation is an important matter and has recently received a good deal of discussion. It will be recalled that for some years intermittent venous occlusion has been recommended as a means of establishing a collateral circulation, in connection with various sorts of arterial obstruction and deficiency. Linton, Morrison, Ulfelder, and Libby⁴¹ demonstrated to their own satisfaction in the experimental animal that occlusion of the principal vein of a limb induced increased

arterial pressure in that limb, and that there were relations between the point at which the occlusion was made, and the length of time it was maintained, with the degree to which arterial pressure was elevated. The whole matter is related to the circulatory balance, which has long been regarded as of fundamental importance when large arteries must be sacrificed. The observations of these writers were consistent with the practice of dividing the companion vein at the same level as the arterial section or higher. More recently, Friedland, Hunt and Wilkins⁴² have measured the arterial flow in the extremities of human beings with and without the venous congestion produced by inflating a blood-pressure cuff on the proximal part of the limb. They tested the flow by various methods and found that it was not increased in the limbs during the rise of venous pressure but on the contrary was usually decreased. This subject comes up acutely, of course, in these war times when a wounded limb is on the borderline of gangrene as a result of a serious arterial injury. Ligation of the companion vein, hitherto regarded as essential, may prove to be less important than intermittent depression of the level of the wounded limb, the idea being to secure some degree of venous engorgement without bringing on a harmful edema. "Intermittent venous occlusion" in treating various sorts of arterial deficiency in the lower limbs is still on trial.

THROMBOSIS IN VARIOUS VEINS OF THE BODY

Idiopathic recurrent thrombophlebitis. Bucy and Lesemann⁴³ report a remarkable case of recurrent thrombophlebitis in which the condition was exhibited over a period of fifteen years in various parts of the body. The disease had shown itself, previous to the most recent episode, in both legs and one arm. Finally it involved some of the cerebral cortical veins and the retinal veins of the right eye. Associated with this attack was an acute subdural hemorrhage, requiring evacuation of the hematoma. The patient recovered. The literature is summarized.

Mesenteric thrombosis treated with heparin. Luke⁴⁴ reports a case of venous mesenteric thrombosis in a soldier of forty-two. The history and physical examination were typical. Exploratory operation disclosed thrombosis in the mesenteric veins serving about 135 cm. of small bowel. The intestine appeared barely viable. The patient recovered under heparinization.

Septic thrombosis of cavernous sinus. Schall⁴⁵ reports 3 patients suffering from cavernous sinus thrombosis of the anterior type, with staphylococcal bacteremia, successfully treated by sulfathiazole and heparin. Sulfathiazole was given in sufficient dosage to maintain a blood level of 5 mg. per 100 cc. and was continued for a long period after the administration of heparin was discontinued. Schall discusses the theoretical value of this combination, as suggested by Lyons,⁴⁶ and the possible use of

sulfonamides other than sulfathiazole. Apparently the principle of combining heparin with a sulfonamide is a sound one.

VARICOSE VEINS

It is to be observed that the tendency evident in previous progress notes on varicose veins has continued. Papers are appearing describing technics for sclerosing injection, but on the whole the study of etiologic factors and of the interrelation of varicose veins and venous pressures has been more in evidence. In 1942, favorable comment was made on Adams's⁴⁷ communication discussing pressure in varicose veins as compared with normal veins of the lower extremities. Adams showed that, in the standing position, pressure in both sorts of vessels was equally due to gravity alone, unless coughing or straining occurred. Then, pressure in the valveless varicose veins rose even to arterial heights, whereas in the well-valved femoral system this extra rise failed to occur. One corollary of his work was to belittle the value of elaborate tests for incompetent communicating veins, "blowouts" and so on, since adequate high ligation prevents the rise of pressure in varicose veins below the interruption, due to straining, and pressure in such veins, which are connected only with the valved femoral system, continues to represent the effect of gravity and of gravity alone, whether or not communicating veins are also interrupted. Another significant communication was that of Veal and Hussey,⁴⁸ who found elevated pressures in the popliteal veins of pregnant women, showing how functional incompetence of valves explains the well-known causal relation between pregnancy and varicosity. In this connection, it will be noticed that Adams advised the addition of straining to the Trendelenburg test, which ordinarily records the effect of gravity only, for by that means the actual clinical competence of the varicose veins to forward blood and resist high back pressure can be determined.

Etiology. Eger and Casper⁴⁹ believe that since there are no valves in the vena cava and common iliac veins, it is the role of such valves as are present in the external iliac veins to support, proximal to the legs, the long column of venous blood. Actually, these valves are inconstant, and their absence imposes a greater than natural burden on those in the femoral system below. If valves in the common femoral vein are also wanting, the saphenous, as well, is directly exposed to high back pressures. In 7.9 per cent of their cadavers, Eger and Casper found a bilateral lack of valves above the orifice of the great saphenous, and in 35.8 per cent absence of valves on one side or the other. Only one valve is likely to be present in any case above the great saphenous. There was no valve on the right in 10.4 per cent and on the left in 18.5 per cent. They conclude that if lack of valves is the etiologic factor, varicosities should develop unilaterally in 29 per

cent and bilaterally in 8 per cent of all persons. The left leg should show varicosity twice as often as the right. Another possible etiologic factor is an obstructive anomaly at the mouth of the left common iliac vein, to which attention is called by Krumbhaar and Ehrlich.⁵⁰ This they found present in 30 per cent of 280 autopsies.

Pathologic physiology of varicosity. Chapman and Asmussen⁵¹ bring up a subject as to which I have always been curious. I have expected to meet some time a patient suffering from extensive varicosities who experienced faintness on standing up, owing to the rapid downpouring of blood into capacious valveless veins. Actually I have never encountered this phenomenon, but Chapman and Asmussen go at the problem in a more scientific way. Starting with the fact that even normal persons are likely to accumulate in their lower limbs some 500 cc. of blood when standing still (over and above the amount which is present in the horizontal position), and recognizing the diminished output of the heart that has been observed to result, they have investigated some of the logical effects of the even greater downpour of blood into greatly dilated varicose veins. They find that, as compared with normal persons, those having large varices suffer a fall of cardiac output four times as great, a greater lowering of systolic blood pressure and a more marked increase in the pulse rate. After high interruption of the varicose veins, these tendencies are for the most part corrected. Patients suffering from shortness of breath, dizzy spells and faintness are greatly relieved. It is to be noted, however, that not all patients in whom the cardiac output is lowered excessively by the assumption of the upright position make any actual complaints. It appears therefore that only those on the borderline of cardiac incompetence are consciously suffering from the pooling of their blood in varicose veins. The authors note also an increase in blood volume in the varicose patient.

Venous pressure in the presence of varices has also been studied by Mayerson, Long and Giles.⁵² Aware of the investigations of both Adams and the authors just quoted, they reason that since the vascular bed, in the presence of varicosity, is greatly enlarged, there must be a concomitant increase in blood volume similar to that of hyperthyroidism, cardiac disease and arteriovenous fistula. Thus, when the varicose patient assumes the horizontal position, his vessels contain more blood than he needs and consequently venous pressure rises. They show this high pressure to be present in the arms as well as the legs in their recumbent patients.

Such considerations as these bring up the rather interesting point whether high ligation without actual obliteration of varicose veins does for the borderline case all that might be accomplished in the way of reducing the capacity of the vascular bed. Partly with this point in mind, I carry out a low-

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30281

PRESENTATION OF CASE

A seventy-five-year-old housewife entered the hospital because of abdominal pain.

The patient had been in apparent good health until three or four months before admission, when she had the "grippe" for several days. Following this she felt poorly. During the week before entry she had extreme constipation, relieved by high colonic irrigations, and accompanied by considerable anorexia and frequent vomiting. On the evening of admission she suddenly had severe epigastric pain, went into collapse and sweated profusely. She was seen half an hour later. She had severe epigastric pain, which did not radiate, associated with considerable retching and vomiting. The vomitus consisted of clear frothy material. The neck veins were distended, but the venous pressure as measured by raising the arm above the level of the heart was not elevated. The pulse was rapid and weak. The blood pressure, which on one occasion had been recorded as 180 systolic, was found to be 130 systolic, 70 diastolic. After about one hour the pain subsided and she was sent to the hospital.

The patient had had Paget's disease of the bone for many years, without any skull enlargement. For several years she had had one good meal daily but the diet had not been well balanced. Five years before entry she apparently had a similar episode of epigastric pain, which was treated by her physician.

Physical examination on admission showed a poorly nourished, pale, dehydrated woman. The lungs were clear. The heart was enlarged to the left and the sounds were forceful and regular. There was tenderness in the right upper quadrant and in the epigastrium. The liver edge was palpable.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 97.6°F., the pulse 110, and the respirations 25.

Examination of the blood showed a white-cell count of 21,800, with 87 per cent neutrophils. The red-cell count was 3,430,000, with 9.5 gm. of hemoglobin. The urine had a specific gravity of 1.010 and gave a ++ test for albumin; the sediment contained 6 red cells and 12 white cells per high-power field and occasional coarse granular casts.

Plain films of the abdomen showed all the bones to be markedly decalcified, with coarse trabeculations. Along the brim of the left side of the pelvis there was cortical thickening suggestive of Paget's disease. The kidneys and psoas contours appeared normal. There were no dilated loops of intestine.

X-ray films of the chest showed the lung fields to be radiant. The chest was deep. The pulmonary markings were somewhat prominent. The diaphragm was somewhat depressed. The heart was enlarged in all diameters. The aorta was moderately tortuous.

The evening of admission the patient had a second attack of pain. This time the pain was in the right upper quadrant and radiated to the right shoulder. She became cold and clammy, with a rapid and weak pulse. The blood pressure remained unchanged. The pain was relieved by 1/6 gr. of

*On leave of absence

morphine. During the night she had two more similar attacks. In the morning she continued to have tenderness in the epigastrium. The neck in the thyroid region seemed swollen. She spoke as if she had a "hot potato in her mouth," and she stated that her throat felt sore. An ice collar applied to the neck and hot gargles seemed to bring about some regression of symptoms.

Twenty-four hours and thirty-six hours after admission the patient had two other attacks of pain in the right upper quadrant radiating to the shoulder. Examination was essentially as before, with the addition of some stridor, which was relieved when she was propped. The pain was relieved by morphine. She was given intravenous fluids and 100 cc. of blood. There was some difficulty in getting into the veins because they were collapsed. On the second hospital day, about forty-eight hours after the onset of her illness, she seemed better and more cheerful but suddenly went into collapse and died.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: Let us look at the x-ray films.

DR. GEORGE W. HOLMES: The bones show the characteristic decalcification found in aged people. There is nothing in these films to suggest Paget's disease, and that diagnosis must have been made on the basis of other films. There is marked increase in the anteroposterior diameter of the chest, which one often sees in cases of emphysema, and in the other view of the chest the lungs are moderately bright and not inconsistent with this finding. The impression one gets from reading the report is different from that gained from these films. The heart is enlarged, but not strikingly so. There is a good deal of calcification in the bronchial tree and along the line you see here, which is rather confusing. The supracardiac shadow is wide. It does not give the impression of any great degree of tortuosity. There is a shadow above the aorta that could be the root of the innominate artery. Dilatation of the root of the innominate does occur when there are lesions of the aorta itself. In this lateral view the outline of the aorta is not sufficiently clear for me to decide whether it is abnormal. I am surprised that it does not show better. With a normal aorta in a patient of this age, one would expect to see its outline better than one does in this film.

DR. ALLEN: There are a number of things about this record that I question, and it would be helpful to have considerable additional information.

Obviously this case must have been considered as a questionable acute abdominal emergency, although there is no note to that effect. The first thing that interests me is that until the patient had what was diagnosed as "grippe" she had been well, and after that she had not been well for a period of three or four months. I do not know what kind of illness this was. The term "grippe" covers a mul-

titude of disorders. It does not say whether she had gastrointestinal symptoms at that time, although people occasionally classify some types of gastroenteritis under the general heading of grippe. The record does not state whether the patient had any fever through the months before her acute illness. It is possible that she had a low-grade fever with her prolonged malaise.

The week prior to entry she had extreme constipation, which is not unusual in a woman of seventy-five who is as thin as the x-ray films show this patient was. These elderly people frequently have obstipation. We are told that the constipation was relieved by high colonic irrigations, so it appears that this episode five days prior to entry was not due to intestinal obstruction. The severe sudden pain probably was not associated with the colonic irrigation. I assume that it was not because I think that it would have been so stated if there had been any relation. Of course, sudden severe abdominal pain from perforation of a diverticulum or from perforation of a weak spot in the bowel sometimes does follow irrigation of the colon. The pain was sudden and severe and in the epigastrium. She went into collapse and sweated profusely, and her physician apparently saw her within half an hour. He obviously was impressed with the fact that she was quite ill, because as soon as he could arrange it, she was brought to the hospital. They state that the epigastric pain did not radiate, and that may have been true. It is possible that she was in considerable shock either from pain or from the trouble that had brought on the pain; if so, she might not have been able to differentiate too well whether the pain started in the epigastrium or to where it radiated. She did have retching and vomiting, however, which probably arose not from the pain or from the morphine but from the lesion itself.

The statements that the neck veins were dilated and, later, that there was swelling in the thyroid region bother me a great deal and I have difficulty tying those together with the rest of the picture. They may be important in the differential diagnosis, but I am unable to link them up with the lesion that I believe this woman had.

She had a drop in blood pressure, which indicates shock, and farther on we see that the red-cell count was 3,500,000, with 9.5 gm. of hemoglobin, indicating the possibility of blood loss. Later in the record we see that she had been having one meal a day, and it is stated definitely that the diet was deficient; so possibly, and quite probably, the red-cell count and hemoglobin were about as reported, even before the episode of acute illness came on. One of the important pieces of data that we are given is the leukocytosis of 21,800, with a differential count of 87 per cent neutrophils. It is unusual to get that amount of leukocytosis with an elevation of the neutrophils on the basis of anything else except inflammation or gangrene. To be sure, it does occur with some of the other conditions,

woman had had no injury, and we have no reason to suppose that that was what she had. Bleeding into the peritoneal cavity from a ruptured aneurysm or ectopic pregnancy will cause some elevation in the leukocytes, but not to this degree. Mesenteric thrombosis produces extreme leukocytosis, but Dr. Wyman Richardson has recently told us that an elevated leukocyte count in mesenteric thrombosis is not often associated with an increase in the ratio of the polymorphonuclear cells. None of the surgical service were aware of this, and the one patient on whom we have had an opportunity to test this point since we received the information was apparently an exception to the rule because she had the same elevation of neutrophils that the patient described here had.

Could the "grippe" have actually been an endocarditis? Did she go on for a period of three or four months and then develop thrombi that were given off and finally went into the arterial circulation of the mesentery? This would explain the entire picture in spite of the fact that we have no evidence of a distended bowel in the flat film of the abdomen. One early x-ray examination may be of no particular value. We have little in the record telling us about the final examination so far as the abdomen is concerned. The suddenness of the onset, the severity of the pain, the associated vomiting, which was nonfecal, and the high leukocyte count, — in mesenteric thrombosis it may be much higher than it was in this patient, — all occurring three months after some kind of illness, may form the basis on which to reconstruct this case. The difficulty is that she lived a little long for mesenteric thrombosis of the usual progressive type. Also, it states that on the second hospital day, forty-eight hours after the onset of the illness, she seemed more cheerful but suddenly collapsed and died, which suggests further progression, either perforation of a hollow viscus or something that had to do with the cardiovascular system.

I shall leave the discussion at this point and say that this patient had arteriosclerotic disease and Paget's disease, with all due respect to Dr. Holmes. Also, there was an acute affair, which, I believe, is more likely to have been mesenteric thrombosis than anything else. Of course one must consider the possibility of other acute diseases that involve the upper abdomen, such as perforated ulcer, which would be all right for the length of time she lived, or acute cholecystitis. Patients do not die suddenly from acute cholecystitis; but, when they do, it is usually within a few minutes after the gall bladder ruptures.

DR. CHESTER M. JONES: This patient's symptoms were interesting in that they were referable to the throat and that she had swelling there. Can you tie those facts in with the symptoms of the abdomen? It seems to me that she died of symptoms referable to the neck.

DR. ALLEN: They say that there was definite improvement following the application of an ice collar. I cannot tie the neck symptoms with those of the abdomen. Have you any idea?

DR. JONES: No, except that she had swollen neck veins, which suggest something vascular.

DR. J. H. MEANS: The neck bothered me a good deal. I could not laugh it off, nor could I hook it up with the abdominal diagnosis unless it was on a vascular basis. The story of sudden onset, of doing better and suddenly dropping dead makes one wonder if she had a cerebral embolus. Dr. Allen has suggested the possibility of endocarditis, which is a good one. If she had had one embolus going to the mesentery, she could also have had one going to the cerebrum and causing sudden death. The findings in the neck associated with sudden death remind me of a case that I discussed in which there was sudden demise during a thyroid operation, which turned out to have been due to a cerebral embolus. It seems to me that it is easy to hook up the various phenomena present here on the basis of some kind of cardiovascular or vascular lesion, but precisely what, is difficult to say. Knowing the department's diabolical ingenuity in framing us, and since the first case discussed today was a dissecting aneurysm, I wonder if they might have lined up two dissecting aneurysms for us. It is conceivable, although I am throwing the suggestion out very cautiously.

DR. JACOB LERMAN: When I first saw the patient it was quite obvious that she was in shock. She was exquisitely tender over the epigastrium and had recurring attacks of pain, which finally shifted to the right side. My attention focused on the gall bladder. Consequently I had a surgeon see her, who agreed it was probably an episode of acute cholecystitis. He did not advise surgery, however, because her condition was so poor. She had an anemia, which was greater than that indicated by the red-cell count of 3,500,000, because she was dehydrated when the count was taken. I also was disturbed by the distended veins and by the swelling of the neck, which was definite and did not recede until an ice collar was applied. I raised the question of acute thyroiditis. It was difficult to explain the swelling of the neck and the stridor. The latter improved on elevation of the head. We thought that these symptoms were secondary to throat infection, and let it go at that.

CLINICAL DIAGNOSES

Acute cholecystitis, with perforation?
Paget's disease.

DR. ALLEN'S DIAGNOSES

Mesenteric thrombosis (secondary to subacute bacterial endocarditis).
Arteriosclerotic disease.
Paget's disease.

ANATOMICAL DIAGNOSIS

Aortic aneurysm (? syphilitic), with rupture into mediastinum and right pleural cavity and hemorrhage into soft tissues of neck and walls of esophagus and stomach.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this patient showed an extremely interesting lesion. When we opened the abdomen, the first thing that struck us was the marked hemorrhagic appearance of the surface of the stomach. There was no free blood in the abdominal cavity; the blood appeared to be in the wall of the stomach, extending down from the cardia to about the beginning of the antrum. When the chest plate was removed, about a liter of fresh blood was found in the right pleural cavity, and this hemothorax was undoubtedly the cause of the sudden exitus. The source of this hemorrhage was a perforation of an aneurysm of the descending thoracic aorta. The entire mediastinum was filled with blood clot, some obviously very recent from the terminal rupture and some definitely older. It was this older blood that had apparently been oozing from a subacute perforation of the aneurysm and had extended up into the neck. We found a huge amount of blood surrounding all the vessels of the neck and compressing the esophagus. The blood had permeated through the outer coat of the esophagus and had extended as a hematoma between the muscle layers and the adventitia. When it reached the stomach, a large part of the blood entered the muscle layers of the stomach and appeared as a submucosal hematoma, which bulged into the lumen. The appearance was not unlike that seen in intramural tumors of the stomach, such as leiomyomas and neurofibromas. The aneurysm was saccular, measured 6 cm. in diameter and was probably syphilitic in origin. There was no dissection of the aorta.

In retrospect, the peculiar appearance of the aorta in the x-ray film that Dr. Holmes mentioned was of some significance.

DR. HOLMES: The x-ray appearance may be explained on the basis of the pathology demonstrated. The enlarged root of the aorta and the absence of the shadow of the descending aorta in the lateral view were in all probability due to the blood surrounding these vessels.

CASE 30282

PRESENTATION OF CASE

A twenty-five-year-old woman was admitted to the hospital because of bleeding from the nose and the gums.

The patient had apparently been well until the age of seventeen, when she developed recurrent attacks of sneezing and shortness of breath over a

period of one year. She experienced considerable fatigue and lost about 30 pounds in weight. She was admitted to a community hospital, where diagnoses of bronchial asthma, chronic sinusitis and bronchitis were made, and she was treated with ephedrine and potassium iodide. Many skin tests were positive and she was advised to regulate her habits accordingly. She was discharged but re-entered that hospital five months later because of nausea and vomiting of two weeks' duration. The blood pressure was 150 systolic, 105 diastolic. The white-cell count ranged between 10,000 and 20,000, with an eosinophilia of 6 to 30 per cent. While in the hospital she developed anemia. The urine showed albumin, red cells, white cells and hyaline and granular casts. One serum protein determination was reported as 9.1 gm. per 100 cc. A diagnosis of periarteritis nodosa was entertained, but a muscle biopsy was negative. The symptoms apparently cleared up; she was discharged after two months in the hospital and remained symptom free for about a year. At the end of that period, following an upper respiratory infection, she had recurrence of the asthma and re-entered the same hospital. Examination showed expiratory and inspiratory wheezes and groans, but no rales or dullness. The blood pressure was 160 systolic, 125 diastolic. The urine concentrated as high as 1.032 and showed a variable amount of albumin. The sediment almost constantly revealed 1 to 2 red cells, 2 white cells and 5 to 20 coarsely granular and hyaline casts per high-power field. The total urine albumin output varied from 2.6 to 18 gm. Phenolsulfonephthalein excretion tests were all in the neighborhood of 25 per cent of the dye in two hours. Both kidneys showed equally poor function, but cultures were negative. The blood nonprotein nitrogen varied from 49 to 26 mg. per 100 cc., and the total protein was 7 gm., with an albumin of 3 to 4.7 gm. and a globulin of 2.7 to 3.4 gm. The blood calcium was 12 mg. per 100 cc., and the blood phosphatase 4.4 mg. The asthma was rapidly brought under control. She was asymptomatic, but displayed little if any improvement in the kidney function and was finally discharged on the fifty-seventh hospital day. Following discharge she felt well until one and a half months before admission to this hospital, when she contracted an upper respiratory infection. Her nose started to bleed; at first the bleeding was spotty, but then it gradually increased. The bleeding occurred without any apparent exciting cause every two or three days and lasted for two or three hours. One month before entry bleeding from the gums was noted which was most marked from the region of the molars and alternated from one side of the mouth to the other. This continued for five or six hours at a time and was occasionally temporarily alleviated by the application of Dermital lotion and alum. The bleeding was more apt to occur at night, when she would wake up with a

mouthful of blood. During this period she noticed an itching sensation in the eyes, black and blue spots on the legs and, for two weeks before entry, swelling of the ankles, which disappeared with bed rest. She missed one menstrual period at the onset of this illness, and the second one, which started eight days before entry, was associated with much pain and many large clots, neither of which was normal. She had had some morning nausea without vomiting, but denied any possibility of pregnancy. Her physician had given her calcium gluconate without any effect.

During this six-year period she had had no fever except that associated with upper respiratory infections; she had also had no chills, joint pains, dysuria, hematuria, pyuria, incontinence or increased frequency. She had had measles, diphtheria, bronchitis and influenza as a child. Following diphtheria, at the age of fourteen, she had "kidney trouble," which kept her in bed for many months.

Physical examination showed a well-developed, moderately undernourished pale woman in no distress. A small amount of blood oozed from the nose. Some coagulated blood was present on the gums. A few squeaks were heard over the lung fields. The left border of cardiac dullness was 11 cm. to the left of the midline in the fifth space. The first sound was loud, and there was a grating early apical systolic murmur. The abdomen was negative. Numerous black and blue areas were present on both thighs. No skin nodules were palpable.

The blood pressure was 172 systolic, 98 diastolic. The temperature was 99°F., the pulse 112, and the respirations 22.

Examination of the blood showed a red-cell count of 1,420,000, with 50 per cent hemoglobin. The white-cell count was 6300, with 58 per cent neutrophils, 17 per cent lymphocytes, 6 per cent monocytes and 12 per cent eosinophils. During her entire stay, except as noted, the urine had a reaction of pH 6.0 and a specific gravity of 1.010. It showed a +++ test for albumin, and the sediment contained occasional white and red cells. A blood Hinton test was negative. The blood nonprotein nitrogen was 129 mg. per 100 cc., and the protein 6 gm. The prothrombin time was 21 seconds (normal, 18 seconds).

She was given blood transfusions. Various measures to control the bleeding were at first unsuccessful. She was placed on a high-vitamin and high-calorie diet. On the fourth hospital day the blood chloride was 117 milliequiv. per liter, and the sodium 146.8 milliequiv. The blood calcium was 9 mg., and the phosphorus 3.1 mg. per 100 cc.; the carbon dioxide combining power was 9.9 millimol. per liter. An x-ray examination of the chest showed rather diminished linear shadows behind the heart and the left hilus. The heart size was within normal limits. The aorta was more tortuous than usual.

On the seventh hospital day a gallop rhythm was heard. In addition, one or two observers heard mid-diastolic rumble. An electrocardiogram showed a normal rhythm of 90. The PR interval 0.20 second, and T_1 , T_2 and T_3 were upright. QR demonstrated slight tendency to low voltage. The axis was normal. The patient was placed on a daily regime of 3 gr. of digitalis, a fluid intake of 1700 to 2500 cc., 0.8 to 1 gm. of protein per kilogram of body weight, 7 to 10 gm. of sodium chloride, and 3 to 5 gm. of sodium bicarbonate.

On the thirteenth hospital day intermittent bleeding from the gums was noted, which was temporarily controlled by adrenalin packs, fibrin foam and raw beef and she was transfused with blood. The urinary output was 1000 cc. on an intake of 200 cc. The pH of urine was 6.5, and it gave a ++++ test for albumin. A blood nonprotein nitrogen was reported as 35 mg. per 100 cc. the chloride 107.1 milliequiv. per liter, and the carbon dioxide combining power 15.7 millimol. per liter. The sodium was 141.8 milliequiv. per liter, and the calcium 8.8 mg. per 100 cc. On the fifteenth hospital day the patient had considerable gastric discomfort, which was relieved after digitalis was stopped. In the course of the next few days she experienced headaches, dizziness, and pain and light flashes in the eyes. Fundal examination showed spasticity and narrowing of the arteriole without any exudate. A blood nonprotein nitrogen five days after the preceding determination was 34 mg. per 100 cc., and the carbon dioxide combining power 23 milliequiv. per liter. These two low nonprotein nitrogen determinations occasioned much confusion and mystification and premature rejoicing at the wonders of modern therapy until a repeat nonprotein nitrogen, six days later, was found to be 129 mg. per 100 cc. Because of the persistence of the intermittent bleeding from the gums which was sometimes fairly profuse, various dental measures, such as extraction of certain of the teeth and correction of faulty occlusion, were contemplated but deemed inadvisable. On the thirtieth hospital day, the nonprotein nitrogen was 164 mg. per 100 cc., the chloride 96 milliequiv. per liter and the carbon dioxide combining power 16 millimol. per liter. A blood urea nitrogen was 142 mg. per 100 cc. Two urea-clearance tests were 41 and 55 per cent normal. A phenolsulfonephthalein test showed no excretion in two hours. The urinary output was between 250 and 750 cc. daily on an intake of 1500 to 2000 cc. The pH of urine was 7.1 to 7.5, but the urinalysis was the same as before.

On the forty-second hospital day she developed anorexia, nausea, vomiting, increasing headache and dizziness, weakness, and bleeding from the gums and nose. She started to wheeze, ankle edema appeared, and there were transient episodes of numbness of the legs. A precordial friction rub was heard. The abdomen became distended. The urinary out-

It was below 250 cc. on an intake of 1500 cc. The nonprotein nitrogen was 186 mg. per 100 cc., the chloride 96 milliequiv. per liter, and the red-cell count 1,660,000. The nonprotein nitrogen gradually rose to 250 mg. per 100 cc., the chloride fell to 83 milliequiv. per liter, the blood protein remained over 6 gm. per 100 cc., and the calcium was 9.6 mg.

On the fifty-fourth hospital day the patient had a scattered papulopurpuric eruption on the face and trunk and considerable itching. Nausea and vomiting of dark-brown material continued, and she developed diarrhea; the precordial friction rub became extremely loud. She died on the fifty-ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: This seems clearly to be a case of progressive renal failure terminating in uremia, with classic signs and symptoms. The somewhat temperamental nonprotein nitrogen level seems unnecessary for making a diagnosis of terminal uremia in view of a number of other observations, namely, hypertension, hemorrhagic diathesis, friction rub, anorexia, vomiting and diarrhea. We may therefore check off those findings in the case that are characteristic of renal failure and proceed to consider its etiology.

The question to be answered is, Was this a primary or localized disease of the kidney, or was it part of a more generalized disease, as was suggested in the hospital to which the patient was admitted some years ago?

On reading over the case the course of the disease appears to be that of a chronic glomerulonephritis following acute glomerulonephritis, with an acute exacerbation in the interval that has been described in detail. The first suggestion in the history that the patient had kidney disease occurs when she was said to have been confined to bed following diphtheria. It is worth pointing out that the type of acute kidney disease that progresses to chronic nephritis is rare following diphtheria and is frequent following streptococcal infection. We must consider that she possibly had a streptococcal infection along with the diphtheria or that in reality she had a streptococcal infection, if we are to take this seriously as part of the history. This was followed by a course which, so far as we are able to tell from the history, was characterized at times by a moderately elevated blood pressure, with a high diastolic pressure. Later, there was evidence of cardiac hypertrophy, clinically but not by x-ray examination, and evidence of change in the aorta beyond what is normal for her age.

The urinary findings showed albuminuria and red and white cells and casts in the sediment, the cells having been at all times apparently moderate in number. She showed a progressive anemia toward the end of her course. There appears to be a

plethora of laboratory findings, some of which are difficult to interpret. In particular, I should say that the terminal observation that the urea clearance was half of normal, whereas the patient failed to excrete phenol red during the course of the two hours, appears paradoxical. It seems clear that the patient had acidosis at her final admission, and the therapy for this acidosis was fairly successful. It also appears that some cardiac failure was present terminally, although the x-ray studies failed to show enlargement.

Regarding the probable anatomic findings, the presence of considerable albuminuria in the last stage of this condition suggests that the patient had not reached the stage of the very contracted kidneys of an extreme terminal, chronic glomerulonephritis.

With regard to the differential diagnosis of disease localized in the kidney, there seems to be little in this case to suggest another diagnosis. The absence of fever and chills and the extremely long course are against focal embolic nephritis from endocarditis, although cardiac murmurs were noted and they may have changed in the course of observation. There is no good evidence for pyelonephritis, and at one time a culture of the urine was made and found to be negative. Polycystic kidneys would hardly occur without a palpable mass on at least one side. I think that similarly obvious considerations are against renal tuberculosis and amyloidosis.

Regarding general diseases in which the renal phenomena may be prominent, although the patient had eosinophilia, anemia and a bleeding tendency, there is no special reason to assume the presence of leukemia, Hodgkin's disease or some other tumor that happened to involve both kidneys and the bone marrow.

I should like to consider why periarteritis nodosa was entertained as a possible diagnosis on the previous admission. Presumably this was because, in addition to the nephritis and hypertension, the patient had a high total protein and eosinophilia. Some consideration might also have been given to the pulmonary symptoms, suggesting that she had arterial disease involving the lung. There is, however, no evidence of a positive sort for this diagnosis, attractive as the thought might have been that such a diagnosis could be made during life. The fact that the patient apparently recovered during the interval between the previous admission and the present one is not necessarily against the diagnosis of periarteritis nodosa, because periarteritis nodosa does undergo remissions. Is there any possibility that the patient had periarteritis nodosa on the basis of sensitivity to sulfonamide drugs? All it is possible to say is that we have no evidence that the patient was subjected to sulfonamide therapy, although she had had a great many infections, particularly upper respiratory infections. It is entirely possible that such therapy may have

been given from time to time and forgotten. On the other hand the previous trouble occurred several years previously, possibly before sulfonamides were in common use. I therefore think that the diagnosis of periarteritis nodosa or other generalized vascular disease ought to be considered improbable, and that it is reasonable to make a diagnosis of chronic glomerulonephritis. If there is a radiologist here, I should like to have him comment on the diminished linear shadows in the chest.

DR. JOSEPH B. AUB: Is the lateral spine normal? Are the vertebrae normal?

DR. BENJAMIN CASTLEMAN: There is no radiologist here.

DR. WYMAN RICHARDSON: This patient was on the service for almost two months when I was visiting. We reached the same conclusion that Dr. Brues has, namely, that she had chronic glomerulonephritis. We simply toyed with the idea of periarteritis nodosa. She had an enlarged heart, and I do not know why it does not show by x-ray. She had a definite gallop rhythm, and we had the usual futile discussion concerning mid-diastolic murmurs. I was very much on the fence in this matter of murmurs, and I am quite ashamed of my note in the record. The thing that troubled the girl the most was the bleeding, and it also troubled me a great deal to explain it, although it is frequent with renal failure. It is suggested that the bleeding is due to toxic damage, whatever that may mean.

DR. BRUES: I see no mention of platelets.

DR. RICHARDSON: They were numerous.

I found it difficult not to take a completely defeatist attitude in regard to therapy and decided to send the girl home when the bleeding seemed to stop somewhat. The service felt that we ought to try to correct the chemical situation, which I think was the proper attitude to take. In spite of the fact that the acidosis was considerably improved, I could not see that the patient herself was any better. She went downhill from that point on.

DR. ALLAN M. BUTLER: I was asked to see the patient to render advice whether the bleeding was due to vitamin C deficiency. It was my opinion that a plasma ascorbic acid determination was not worth doing because it would give relatively little information in appraising vitamin C deficiency. For even if the plasma vitamin C were zero, it would not mean that the bleeding was due to a vitamin C deficiency. If, however, the white-cell and platelet content of ascorbic acid were reduced it would mean that the patient was suffering a deficiency severe enough to cause this hemorrhagic tendency. At that time, however, the laboratory was too busy with war work to determine the vitamin C content of the white cells and platelets. I suggested a therapeutic trial of vitamin C. Since the diet did not suggest deficiency, I thought that the bleeding was associated with the hypertension and anemia. I recommended transfusing the patient before re-

sorting to digitalization, and before seeing if sodium sulfate would affect the hypertension. It also seemed to me that an appraisal ought to be made of the renal function before any consideration was given to the desirability of doing a sympathectomy. As intravenous pyelograms had been taken at the other hospital, I suggested that it would be wise to get hold of them to see if any information could be obtained about possible anatomical anomalies that might be behind the renal disease.

The odd nonprotein nitrogen values are a good example of doing quantitative chemistry with technicians who are not expert chemists. The reason these two falsely low determinations were obtained is that the technician who did them carelessly added too much acid so that the final reaction was not alkaline enough and the color did not develop. It is the kind of error that crops in if technicians are not properly trained in the methods of quantitative chemistry.

The final thing is that the lack of blood pressures in the history as recorded here makes it hard to decide what went on in this patient. One wonders how much of the primary difficulty was cardiac failure and how much was due to renal failure.

DR. CASTLEMAN: Two days before she died the blood pressure was 115 systolic, 70 diastolic; the day before she died it was 130 systolic, 75 diastolic.

DR. BUTLER: She was obviously having considerable cardiac failure.

DR. RICHARDSON: She had pericarditis and a friction rub, and probably had ulcers of the bowel. I should like to take exception to something Dr. Butler said. I do not see why the bleeding was due to anemia and high blood pressure. High blood pressure may cause rupture of an artery, but not oozing from the gums and capillary bleeding. Nor does anemia cause it, unless there is a lack of platelets, or except in certain cases of myelogenous leukemia.

DR. BUTLER: You know more about that than I. In my limited clinical experience, purpura in the presence of severe anemia is not uncommon.

DR. AUB: Uremic patients bleed without vitamin C deficiency. One can "pass the buck" by saying it is due to anemia, but they bleed no matter how one explains it.

DR. BUTLER: Rheumatic fever patients may have considerable purpura.

DR. RICHARDSON: That is probably capillary; this is probably capillary bleeding too. I think it is fair to assume that it was due to toxic effect on the capillaries, but after all, this statement does not mean anything.

DR. BUTLER: It is interesting, also, that when I saw this patient, ten days after admission, she did not have any retinitis in spite of the long-standing hypertension. She had constriction of the retinal arteries and thickening of the brachial and radial arteries but no real retinitis.

CLINICAL DIAGNOSIS

Chronic glomerulonephritis.

DR. BRUES'S DIAGNOSIS

Chronic glomerulonephritis.

ANATOMICAL DIAGNOSES

Chronic glomerulonephritis.

Uremia.)

Cardiac hypertrophy, hypertensive type.

Septicemia (*Staphylococcus aureus*).

Endocarditis, chronic rheumatic: mitral valve.

Parathyroid hyperplasia, secondary.

Renal osteitis fibrosa.

Hemorrhages into skin, pleura, lungs, pericardium,

gall bladder, esophagus and ileum.

Acute esophagitis, terminal, uremic.

Acute ileitis, terminal, uremic.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this woman showed a pair of kidneys that weighed 90 gm., one weighing 40 gm., and the other 50 gm.; they had the typical appearance of chronic glomerulonephritis. The surfaces were uniformly coarsely granular, and the cortices were narrow, measuring 2 to 3 mm. Microscopic examination confirmed that diagnosis. Practically every glomerulus was diseased; most of them were completely wiped out and hyalinized,

and others showed characteristic crescents and capsular adhesions. There were foci of tubular dilatation and of atrophy. All parathyroid glands were quite large, weighing together 0.5 gm., which is three or four times the normal weight, and which indicates that the renal insufficiency had been going on for a long time. Further corroboration of that was the fact that the bones showed early osteitis fibrosa. Quite possibly the vertebrae were a little osteoporotic, Dr. Aub, because the intervertebral disks, as you can see from this roentgenogram, are ballooned out, suggesting that the bones themselves were soft. Some marrow spaces were completely replaced by connective tissue, which was also present along some of the bone trabeculae. This is a mild form of the lesions one sees in a child with renal rickets.

There were numerous hemorrhages throughout the body, including the lungs. If these pulmonary hemorrhages became confluent, I wonder if they might produce the picture in x-ray films that the radiologist calls edema associated with nephritis.* There were recent ulcers, probably on a uremic basis, of the small intestine, not of the colon, which is more frequently involved in uremia, and also ulcers in the esophagus. The heart was enlarged, weighing 350 gm., and the left wall was hypertrophied. The murmur was due to a slight but definite degree of stenosis of the mitral valve on a rheumatic basis; but there was no evidence of acute rheumatic infection.

*Scott, T., Schatzki, R., and Bauer, W. Pulmonary edema: its roentgenologic appearance in acute glomerulonephritis without signs of cardiac failure. *J. A. M. A.* 114 613, 1940

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TRANSFUSION WITH BLOOD AND ITS DERIVATIVES AND SUBSTITUTES

THE stimulus of war has brought rapid advances in the practical application of certain fields of medical knowledge. In no field is this more marked than in the field of transfusion. The tremendous feat of wholesale blood collection, which has been carried on throughout the country by the Blood-Donor Service of the American Red Cross, has conditioned the American people to the donation of their blood and has started, it is to be hoped, a movement that will not cease when the war ends. From the blood that has been collected, a large

amount of dried plasma has been made available for shipment all over the world to the armed forces. Every American on the streets today knows that this has contributed materially to the reduction of mortality from wounds on all the fighting fronts. Recent reports indicate that the red cells, previously wasted, may be resuspended, and distributed to civilian hospitals for administration to anemic patients.

Another development from the Red Cross program has been the large-scale fractionation of human plasma into its component parts by methods developed by Cohn and his associates in the Department of Physical Chemistry at the Harvard Medical School. This work was originally started to provide the armed forces with a compact, concentrated blood derivative for emergency use, particularly by highly mobile military troops for whom transportation space is at a premium. Albumin provides the osmotically active fraction of plasma in a very concentrated form, which can be injected rapidly and safely without reactions, and with a rapid increase in blood volume resulting from the drawing of water from the tissue spaces into the blood stream. The possible uses of such an osmotically active and safe concentrated solution in clinical medicine and surgery are manifold.

The fractionation program provides not only albumin for the treatment of shock and conditions associated with hypoproteinemia but also other globulin constituents of the plasma that have important functions. Two of these products have already found useful applications in the clinic. Fibrin foam, which is derived from the clotting elements of the blood, has been shown to have remarkable hemostatic properties for use in neurosurgical operations. The gamma globulin of human serum has been used successfully for the prevention or modification of measles, its advantages being its availability, reproducibility, potency and freedom from substances producing reactions. Further developments of this program should provide the clinician with many new and useful tools — safe because they are derived from human sources — that can be applied to the treatment of disturbances of normal physiology.

The statement by the Subcommittee on Blood Substitutes of the National Research Council, which appears elsewhere in this issue of the *Journal*, indicates that the same type of careful study has been applied to blood substitutes that have been suggested for clinical use. Every physician would do well to read this statement, since it indicates the degree to which good clinical practice is dependent on the basic sciences. Here he will find a clearcut statement of why, from a physicochemical point of view, gelatin cannot be considered to be a satisfactory substitute for either blood plasma or albumin, although it may have some effect in the amelioration of the diminution of blood volume that characterizes surgical shock. The report emphasizes the dependence of the physiologic function of any material on its molecular size and shape. Gelatin molecules range from very long thin ones, giving rise to certain undesirable properties, such as rouleaux formation of the red cells and their rapid sedimentation, to molecules so small that their fairly rapid escape from the circulation makes the effect of gelatin less sustained than that of plasma. Furthermore, it is pointed out that "gelatin solutions probably do not contribute significantly to nutrition," and their influence on "the distribution of plasma proteins between circulating blood and tissues should be further investigated."

Replacement therapy should be directed, whenever possible, to actual replacement of what has been lost. In the case of shock due to hemorrhage, this means whole blood. For reasons of practicality, however, it has been found expedient to supply the armed forces, not with whole blood, but with plasma and albumin, which will sustain the patient until such time as he can receive the needed red cells in the form of a transfusion of whole blood or of resuspended cells. In certain types of shock, plasma alone is lost, and for these, plasma is the ideal replacement fluid.

The products of plasma fractionation are individual proteins used in relatively pure state for the treatment of specific deficiencies. They are blood derivatives, not blood substitutes and have important properties of their own. Thus, albumin, because of its high osmotic activity may restore

blood volume more rapidly than transfusion of an equivalent amount of plasma. The specific properties of purified proteins deserve further exploration, and these blood derivatives give promise of having widespread use in the clinic.

WARTIME POPULATION TRENDS

THE Metropolitan Life Insurance Company, in its April issue of the *Statistical Bulletin*, publishes some interesting comparisons of wartime population trends among various countries. The Axis countries, suffering increasing battle losses, are also less able to replenish their populations at home. On the other hand, the United States and Great Britain have shown marked gains in the natural increase in their populations since war broke out. Germany, home of the "master race" that seems doomed never to achieve its mastery, has become again the land of the deepening shadows.

Germany's natural increase of population, according to this reliable source of information, has been dropping steadily since the war began, with the decline becoming more marked each year that the war continues. Thus the excess of the birth rate over the death rate dropped from 8.1 per 1000 population in 1939 (the best year under the Hitler regime) to 2.9 in 1942, the last year for which official figures are available. The year 1942 had the distinction of revealing the lowest rate of increase in Germany for any year since World War I. It can be assumed that, since 1942, the large-scale bombing of German cities, with evacuation of populations, and the heavier concentrations of men on the fighting fronts have further increased the death rate and decreased the birth rate. The old warning that whom the gods would destroy they first make mad seems to be proving its worth again.

Italy, a member of the Axis until 1943, likewise showed a drop of some 40 per cent in the excess of births over deaths—from 10.1 per 1000 in 1939 to 6.1 in 1942, a decline largely due to a decrease in the birth rate. The other Axis countries have shown similar, though less marked, trends.

Of the occupied countries, a mixed situation seems to have existed. Denmark showed an increase in the

margin of births over deaths through 1942. In the Netherlands, the rate of increase rose after an initial fall. Belgium and France are facing serious depopulation, with death rates exceeding birth rates since 1940.

The crude rate of natural increase in the United States has risen to its highest figure in twenty years, with Canada's growth a close parallel. In England, the excess of births over deaths in 1943 was over 175,000, the highest in fifteen years. Figures are not available for China and Russia, but it may be expected that their usual high fertility will again prevail with their soil freed of invaders and their armies returned to the land.

Regardless of what we may believe regarding the selective limitation of populations for the future, it is obvious that population trends among the United Nations are showing a normally healthy situation as compared with those of Central Europe.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

CLINIC	DATE	CLINIC CONSULTANT
Lowell	August 4	Albert H. Brewster
Springfield	August 16	Garry deN. Hough, Jr.
Hyannis*	August 22	Paul L. Norton

*Date changed.

WAR ACTIVITIES

NATIONAL RESEARCH COUNCIL

The following statement was recently released by the Subcommittee on Blood Substitutes of the National Research Council.

On the basis of the extensive earlier literature and the recently accumulated evidence, certain statements can be made concerning gelatin solutions prepared for intravenous use and the chemical, physiologic and clinical properties of such solutions compared with those of plasma.

I. Chemical

(1) Plasma is constituted of molecules whose size is known and is related to plasma function. The plasma proteins may be grouped into a few classes, in each of which the molecules are of uniform size and shape. Gelatin and degraded gelatin solutions submitted for study as transfusion fluids show almost continuous variation in size over a very wide range.

(2) Plasma proteins have diameters close to 36 Angstrom units. Most of the particles of gelatin and degraded gelatin have diameters of about half this value, 18 Angstrom units.

(3) The largest part of the plasma proteins do not deviate greatly from symmetrical shape, though fibrinogen, present to a small extent, has long, rodlike molecules. Gelatin appears to be made up of linear polypeptide chains loosely coiled to give very long molecules.

(4) Degradation of gelatin decreases the number of very long particles, which are responsible for the gelation, much of the viscosity and probably other undesirable effects. Degradation increases the number of very small particles, which are responsible for most of the osmotic pressure, though not for

the colloid osmotic pressure since they diffuse rapidly through membranes.

(5) A standard technic of degradation of gelatin yields solutions of about the same average molecular weight and the same size distribution. The degree of degradation is best measured by the number of potential peptide linkages that are broken. This number can be determined from the osmotic pressure, or more easily from the viscosity, since the intrinsic viscosity of these solutions is proportional to the number-average molecular weight.

(6) Plasma proteins do not readily diffuse through membranes employed in measuring colloid osmotic pressure. A large part of the degraded gelatin solutions submitted for study as transfusion fluids are of such small size as to diffuse readily through such membranes.*

II. Physiological and Clinical

(1) *It must be recognized that, when available, whole blood, plasma or human serum albumin are the solutions of choice to be employed in the treatment of hemorrhage or shock.*

(2) It has been demonstrated that when the precautions recommended to the gelatin industry are taken, pyrogen-free solutions of gelatin can be prepared.

(3) Such gelatin solutions have been given to man without late toxic reactions.

(4) A small percentage of patients have been found to have immediate reactions. Local thromboses are common when certain preservatives are employed.

(5) Injection of the gelatin solutions have been made without evidence of sensitization.

(6) Many repeated injections in animals have been given without evidence, histologic or clinical, of toxicity or irreversible accumulation.

(7) The solutions of gelatin studied have a definite effect in augmenting cardiac output and circulating blood volume in dogs submitted to hemorrhage and in patients suffering from shock due to hemorrhage or skeletal trauma. The evidence at present indicates that gelatin solutions may have a beneficial effect in burns. There is thus clinical evidence that these solutions have a definite, though temporary, effect in relieving the state of shock; therefore it is often necessary to take recourse to multiple injections.

(8) The smaller molecules on which the osmotic effects of gelatin solutions depend are rapidly lost from the blood stream, largely through the kidneys. In this respect the effect of gelatin may be contrasted with that of the plasma proteins, which are not normally lost through the kidneys, but when present in excess form reserves in the tissues.

(9) The longer rod-like particles of gelatin persist in the blood stream and are presumably responsible for rouleaux formation, for the increased sedimentation rate of the red cells and for the changes in the distribution of plasma proteins between the blood stream and the tissues.

III. Limitations and Unanswered Questions

(1) *The solutions gel at about 20°C. and therefore cannot be used in cool or temperate climates in the field.*

(2) *Proper typing of blood following the administration of gelatin solutions may be difficult. This problem should be studied further. It may be essential to warn that a sample of blood for typing should be withdrawn from each patient before the administration of gelatin solution.*

(3) Based on present information, the optimal solution mentioned above shows slow but definite and continued degradation at temperatures encountered in certain theaters of war.

(4) The viscosity of the optimal solution is definitely greater than whole blood.

(5) It is not known whether a solution of this type will impair the return of normal function to kidneys in sustained ischemia or in the case of severe burns or the crush syndrome.

(6) Gelatin solutions probably do not contribute significantly to nutrition. Their only place in medical therapy appears to be to restore a loss of circulating blood volume in acute injury of various types.

(7) The influence of gelatin on the equilibrium in the distribution of plasma proteins between circulating blood and tissues should be further investigated.

*The solution with optimal value in the treatment of hemorrhage and shock examined up to the present time is one of 6 per cent concentration, prepared in saline, and with the general physicochemical characteristics of what is known as the "Knox P-20 type."

(Notices on page

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A TOXIC FACTOR IN EXPERIMENTAL TRAUMATIC SHOCK

JOSEPH C. ALB, M.D.†

BOSTON

MEDICAL investigations are often the product of a number of workers. This is particularly so in these years of war emergency, when groups men co-operate in an attempt to solve problems quickly. Thus, in our search for a toxic factor in shock syndrome, credit for the results is largely due to my associates, who have contributed much to the work and many of the ideas. Those who have worked throughout have been Drs. Austin Brues, Nathanson, Alfred Pope and Paul Zamecnik and Miss Abby Nutt; others have collaborated in part of the work, namely, Drs. Waldo Cohn, René Bos, Cynthia Pierce and Seymour Kety and Miss Dorothy Tibbetts. It is in their name that I make this summarizing report.

The history of the study of traumatic shock need only go back to World War I, when a group of illustrious physiologists studied the mechanisms involved in its production. This brilliant work was well summarized in their reports^{1, 2} and in the book Cannon.³ Many of the physiologic responses that constitute the syndrome of traumatic shock were then delineated, and their cause was ascribed to an assumed but unisolated toxin. Subsequent attempts to isolate the toxin failed.

The period that lay between the two world wars was marked by a reaction against the toxic theory because of convincing studies, largely by Blalock⁴ and Phemister,⁵ which showed the predominant role of local fluid loss in the areas of trauma. And so we entered this conflict in the wise belief that the treatment for shock is transfusion, and readily available plasma has certainly saved many lives. Nothing I may say in this discussion should be construed in any way as detracting from this brilliant page of medical and, indeed, social progress.

I need not describe to this audience the clinical picture of traumatic shock. It is the delayed collapse that follows lacerating or crushing wounds, characterized by the well-known drop in blood pressure and diminution of blood volume.

With the onset of this war we again set ourselves to evaluate the possibility of toxic causative factors in shock. But why should one study the causes of shock? Surgeons say that there are many causes of this syndrome, but that point of view may change with further knowledge. It is true that the syndrome may develop from anesthesia alone, or that it may appear in relatively mild trauma or may be lacking in larger wounds. The reasons for this have not been clear, which merely proves that we have not yet learned its causes. Although shock may develop under diverse circumstances, true precipitating factors are probably not numerous. Depletion of the blood volume by hemorrhage will produce shock through obvious mechanisms, but shock — the so-called "toxic shock" — can also apparently arise from causes and through mechanisms that are less well understood. It is as true of this syndrome as of any disease that thorough understanding of its mechanisms is essential to logical therapy. Anyone who has observed the effects of bleeding and of trauma in animals or man is alert to the different toxic appearances of the traumatized animal. Something other than the large plasma loss appears to be involved. But this factor has appeared elusive. Moon⁶ thought that he had found it by the implanting of autolyzed minced muscle tissue in the peritoneum. Scudder⁷ had the ingenious idea that it was due to liberated potassium from traumatized tissues, though we now think that blood potassium rises only late in the shock picture.

The amount of work that has been done in this country on traumatic shock during this war has been large, and our knowledge of the subject is being well advanced. Much of this work is still unpublished and restricted, so that this discussion will be largely limited to recent publications and to our own unpublished data.

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The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Massachusetts General Hospital.

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Professor of research medicine, Harvard Medical School, physician, Massachusetts General Hospital, director, medical laboratories of the Collis P. Huntington Memorial Hospital of Harvard University.

Laboratory studies of traumatic shock have been characterized by the large number of divergent technics and divergent anesthetics in its production. This makes comparison rather difficult. All our observations have been made on dogs with Nembutal given intravenously in amounts sufficient to produce light anesthesia. We have used a new method to produce shock in animals. This was devised as a minimal insult so as not to produce overwhelming shock but to approach the shock state in a more quantitative manner than could be done by technics other than hemorrhage. The method developed by one of our associates, Dr. Nathanson, involves putting tight tourniquets around the two triceps surae, which include the gastrocnemius and soleus muscles. On release of the ties, after five hours, the blood supply becomes re-established and then these muscles swell enormously. The amount of edema that accumulates can be quite accurately estimated by a method, developed by Dr. Kety, of measuring the volume of the limbs.

But fall of blood volume and that of pressure are not the only manifestations of shock that deserve attention. In any experiment it is crucial that other physiologic observations also be made. For blood pressure may be misleading—it may be maintained for a surprisingly long time through vascular constriction, while the shock state may be developing, and then the pressure may fall rapidly, followed promptly by death. Other methods appear essential to judge the early progress of this syndrome—methods that indicate the state of the circulation. Progressive hemic concentration is one of the best technics, as it indicates the actual amount of plasma lost from the circulation. To evaluate the degree of shock we have used technics that originated in the work of one of us (J. C. A.⁸⁻¹⁰) in the last war. It was then shown that when shock is developing the oxygen content of the venous blood is much reduced, that the cardiac output falls, and also that the basal metabolism is reduced owing to the lack of adequate available oxygen. These reactions can all be explained on the basis of a slowing of the blood flow. Our judgment of the degree of shock, therefore, has been based on a fall of cardiac output and blood pressure, a rise in the resistance of the peripheral circulation, mainly that of the arterioles, and a decrease of blood volume. In early experiments we did not obtain all this information, but it has been accumulated in the main body of our recent studies. By means of these technics we were satisfied that we could approach the problem with a quantitative method for producing a minimal shock-producing trauma that would not be so overwhelming as to make study and treatment difficult. We also were able to measure fluid loss in this area progressively, as well as to estimate the beginning and progress of the shock state.

It soon became clear that it would be interesting to study the large amount of fluid that exuded from

the anoxic muscles. A technic for this was arranged by enclosing the muscle in a thin rubber sheath from which the fluid could be collected by simple drainage. After the release of the tourniquet and the re-establishment of blood flow through the muscle, fluid fairly poured out into these investing sheaths. These simple operations could all be done with aseptic precautions, and after our first preliminary experiments, the usual surgical aseptic technics have always been employed.

RESULTS

In the first problem we investigated we sought to find whether the shock state produced a change in the permeability of body cells remote from the area of trauma, that is, whether the cells of organs such as the intestines and the liver allowed electrolytes and proteins to escape more freely than in a normal state. This was an arduous task undertaken by Dr. Brues, in which Dr. Cohn and Miss Tibbetts helped. These data are ready for publication and need no long discussion here. The conclusion was that there was no indication of any consistent shift of intracellular or extracellular water or electrolytes into or out of cells in shock except what occurred locally in the traumatized regions. In the traumatized areas there was evidence that the permeability of cells was considerably altered, so that extracellular salts were allowed to enter and intracellular salts were abnormally lost. Our experiments, however, have shown other characteristics of fluid exchange that appear interesting and important. At autopsy after prolonged shock one finds the intestinal mucosa full of blood, and Dr. Brues has observed that this appears to be markedly increased by transfusion of plasma or blood, showing that transfused fluid may be lost into this area. This indicates that the permeability of these capillaries has been altered by the shock state and that they therefore lose an abnormal amount of fluid.¹¹

It also appears obvious that an abnormal circulation of the body fluids may occur about the area of trauma. Thus, a considerable loss of fluid may exude from the edematous traumatized muscles, sometimes amounting to as much as 200 cc. in five hours. If this fluid is not withdrawn but stays in the legs, it migrates away from the traumatized areas and some of it must be reabsorbed into the circulation. An accessory circulation of fluid is thus established, diffusing through traumatized tissues and being reabsorbed into the general circulation. This may affect the organism as a whole. This circulation, as well as that directly carried in blood vessels and lymph, easily explains the possible widespread effects of the local accumulation of toxic products from trauma. We have established absorption from the anoxic muscle mass by means of radioactive salts. These appear in the blood stream promptly after liberation of the muscle tissue.

have not done this to establish the absorption of free fluid in the wound, but it could easily be done.

The minimal trauma that I have described produced traumatic shock in about a third of the animals. We then measured the fluid that collected from this operation together with the blood that was taken for our various analyses, and compared the incidence of shock in the groups that were subjected to the muscle ties with that obtained in control animals that were bled. There was little difference between the two series. The average incidence of shock in the traumatized animal was higher than in the hemorrhagic controls, but the total loss of fluid in the animals that were traumatized was also slightly higher than that of the control animals. In these observations it appeared that the conclusion of Blalock⁴ and Phemister⁵ was correct and that the shock of trauma was nothing but a large loss of fluid. But we were not satisfied with this conclusion because of the somnolence, lethargy and lack of sensibility to pain seen in patients who have suffered trauma, whereas patients who have simple hemorrhage usually do not exhibit these symptoms so dramatically.

It appeared desirable to investigate the possibility that edema fluids contained some factor toxic to the organism. We therefore collected the fluid that exuded from the muscles that had been made anoxic. This fluid was easily collected aseptically by our technic, although the amount varied markedly in different animals. By using large muscles from which to collect this fluid we could obtain about 200 cc. from one dog. This freshly hemolyzed fluid could then be put into a small test dog to see its effect on blood pressure, diastolic output, peripheral resistance and hemoglobin concentration. By this technic one was increasing blood volume, not decreasing it. If there were toxic, shock-producing factors in this fluid, it had to come along with this increased volume. Interestingly enough, nine out of thirty-two such fluids produced a local traumatic shock in recipient dogs. The results, however, had practically no effect following systemic injection. Drs. Kety and Pope quite wisely inferred from these observations that the toxic factor in these fluids was not constant, and that it therefore probably arose not from the damaged muscle but rather from some extraneous source. This appeared to confirm the old toxic theory of the last war described in Cannon's book³ and the more recent observations of Moon.⁶

We were convinced of a toxic element that was sometimes present in the sheath fluid that exuded from anoxic muscle. We therefore attempted to purify this chemically and, for this purpose, collected more than 2000 cc. of this fluid from a series of 9 dogs. It was collected with sterile precautions in bottles cooled in ice and promptly frozen in

carbon dioxide snow. These fluids were combined, and the mixture proved to be shock-producing to several dogs. It contained some red cells, the hematocrit being about 1 per cent, had a specific gravity of 1.018 and tended to form a thin clot. An analysis of the inorganic salt content of this fluid showed that it contained much intracellular muscle fluid as well as extracellular fluid, for its potassium content was high and its calcium content low. It also contained less protein and more fixed acid than does blood plasma. The toxic factor in this muscle exudate was found to be a large molecule, for it was not dialyzable and was precipitated in the fraction that contained the protein. In this pool of muscle exudate Dr. Zamecnik also found high concentrations of intracellular proteolytic enzymes, and these enzymes were all contained in the fraction of ammonium sulfate precipitate that contained the toxic factor. We therefore sought to find whether these intracellular enzymes might be the factor that produced shock, but subsequent observations proved to Dr. Zamecnik that this was not so, inasmuch as fresh muscle extract that contained the same enzymes in high concentrations did not produce shock. Laborious attempts at purification, therefore, advanced our knowledge only in so far as they showed that the toxic molecule of this accumulation of muscle exudate was in the protein moiety, possibly in the gamma globulins, that it was destroyed by heat, and that its effects were not due to certain enzymes liberated from the damaged muscle. They did not disclose the actual substance that was producing shock in approximately one quarter of the test animals.

In many of these experiments bacteriologic studies of our muscle exudates were made. It soon became clear that, in spite of strict surgical precautions, all the muscle exudates were infected, most of them with organisms of the gas-gangrene group (in muscle exudates from 19 animals, *Clostridia* were found in 13, or 70 per cent). Coliform bacilli were not infrequently present, and in a few experiments *Staphylococcus albus* was found. Bacterial contamination was studied quantitatively to obtain an idea of the number of organisms present. Isolated organisms were also studied by Drs. Dubos and Pierce to see whether they produced toxins. The *Clostridia* were cultured to determine their type, and Dr. Dubos's laboratory found them to be the Welch bacillus (*Clostridium perfringens*).

When the number of these organisms was compared with the toxicity of the fluids, it became clear that the three fluids that produced shock in the series were among those that had the highest concentrations of *Clostridia*. In order to test this finding we assured the presence of an ample infection by injecting a culture of *Clostridia* into the triceps surae muscles at the time of ligation. In a series of 3 animals we injected *Clostridia* that had been isolated in previous experiments. These

muscles produced large quantities of fluid in which the amount of organisms varied as the fluid collection progressed. When the resulting heavily infected muscle fluids were injected into recipient animals, they produced profound shock when only one third of the usual amount of fluid was given. Removal of most of the organisms in the injected fluid was accomplished by high-speed centrifugation. The toxic factor did not appear to be the organism, for the supernatant fluid was equally toxic, whereas injected organisms resulted only in producing fever. A single similar observation was described in a report by the British Medical Research Committee¹² during the last war, in which edema fluid from the injection of *Vibrio septique* produced prompt and fatal shock. We next sought an antidote. Polyvalent *Clostridia* antitoxin was given to a dog a few minutes before injecting an extremely toxic sheath fluid. No shock developed. Our observations indicated that an anoxic muscle was an excellent medium for the growth of *Clostridia* and for the formation of its toxins.

We became interested in ascertaining why our tissues were so frequently contaminated with *Clostridia*. A dog's skin was prepared by shaving and thorough scrubbing with soap and water, followed by ether and alcohol solution, and then painting with strong iodine solution. After this strenuous preparation *Clostridia* could still be found on the intact skin. When Dr. Nathanson used electro-surgical technics with the greatest precaution, *Clostridia* were still found in the muscles deep in the normal anesthetized dog's leg. We are not sure that they exist there normally, for there is a possibility that spores may be carried into the muscle, but it is clear that they are frequently present in muscles in any traumatizing procedure. Our evidence, as well as confirmatory evidence,¹³ demonstrated that *Clostridia* are practically constantly present deep in the skin of dogs. The presence of *Clostridia* has been noted before in dog muscles by Roome and Wilson,¹⁴ although they thought them to be nontoxic. It is possible that they do not produce toxins even though they are present in the normal muscle, and that in traumatized muscles they can multiply and produce their usual toxins only in these relatively anaerobic conditions. This discussion becomes only of academic interest in these observations. The important fact is that the organisms are frequently present in traumatized dog muscle, and whether they are normally present or a contaminant makes little difference in the interpretation of our results. Dogs are the animals usually used for the study of traumatic shock, and the contamination of traumatized muscle by these naturally occurring *Clostridia* appears to us to be significant and to explain our varying cases of shock from muscle juice.

We next turned to the study of purified *Clostridia* toxins. These were obtained through the kindness

of Dr. Milan Logan, who furnished us with the toxins of *Cl. perfringens* and of *Cl. oedematiens*. Injected intramuscularly these toxins produce different reactions. The Welch bacillus (*Cl. perfringens*) produces a great deal of local edema, possibly because its toxin is a lecithinase and therefore has a destructive effect on cell membranes. With this accumulation of fluid in the muscles there develop all the manifestations of shock that we have been determining: a reduced cardiac output, increased peripheral vascular resistance, a fall of blood pressure, a reduced blood volume and its accompanying increased hematocrit, and a lowered venous pressure. All these manifestations may be explained by the local effect of the toxin. We have not yet established whether there is a more general toxic action. When given intravenously this toxin produces marked hemolysis, and although shock is produced, it is different in this regard from our other experiments. We have observed, however, that moderate hemolysis is a common manifestation of shock in dogs, thus confirming the observation of Coonse et al.¹⁵

Cl. oedematiens toxin does not produce edema promptly when given intramuscularly, and intravenously it results in gradual shock without hemolysis. Following the administration of fatal doses there is often no immediate fall of blood pressure. The cardiac output declines gradually to very low levels, with an increased peripheral vascular resistance. The blood pressure falls terminally. At death there is intense congestion of the duodenum and small intestine, the liver is congested, and the adrenal medulla may be hemorrhagic. These findings are analogous to our pathologic findings in shock, except for the hemorrhagic adrenal glands.

The mechanism is known by which the Welch bacillus produces some of its effects.^{16, 17} Macfarlane and Knight¹⁸ showed that the so-called "alpha toxin" is an enzyme—a lecithinase that breaks down lecithin into smaller molecules. Lecithin is a constituent of cell surfaces, so that destructive effects on capillaries or muscle cells can be understood, as well as the hemolyzing effect on red cells. A change of cell surface usually means a change in cell permeability, and so it is possible to explain the large effusions in the muscles where Welch bacillus toxin is placed. A similar enzyme is present in only small amounts in *Cl. oedematiens* toxin.¹⁹ But this is not the only enzyme, for there is also present another group of enzymes called "hyaluronidases" or mucinases, or the so-called "spreading factor," that hydrolyze hyaluronic acid. This acid is found in connective tissue, and the enzymic effect of destroying it results in a great increase of diffusibility through tissue and therefore in the spread of extracellular fluid and bacteria. One may thus explain the great edema not only its presence adjacent to the area of toxic injection but also its widespread diffusion.

Has this work any significance in traumatic shock in the hospital emergency ward or at the front? In a series of eighteen elective orthopedic operations by Dr. Carroll Larsen and others, no Clostridia were found in human muscles. We must therefore decide that any Clostridia present in wounds are introduced at the time of injury. War wounds have been shown to have more than 30 per cent contamination with Clostridia, frequently without the appearance of detectable gas.²⁰ Such Clostridia, introduced into tissues that have not harbored them before, might be expected to be particularly likely to form toxins. The slow onset of shock seen in some of the wounded agrees with the length of time necessary for the proliferation of bacteria and the formation of their toxins. The importance of such organisms in the shock of war wounds appears to be a problem in regions of combat most urgently needing evaluation.

Our experiments have shown again the great importance of a loss of plasma fluid as a cause of traumatic shock, but they also indicate the importance of infection as a toxic factor. Clostridia that lurk normally in the dog multiply rapidly and produce their toxins in the excellent surroundings of traumatized anoxic muscles. The effects there will certainly accentuate the local fluid loss and so give a summation of effects. The toxin of *Cl. oedematiens* in the blood stream produces a shocklike state, but the mechanism is not yet clear to us. The time relations are satisfactory for allowing organisms to grow and for the onset of delayed traumatic shock. We think that the evidence is quite convincing that infection is the so-called "toxic factor" in traumatic shock in dogs.

We do not know as yet how widespread are the effects of the toxin. In our observations in the shocked animal it is clear that elevation of blood volume by transfusion is followed by markedly accentuated local fluid loss in the upper intestine and liver and lungs, as well as in the area of trauma. Such changes in permeability may be due to simple anoxia or to circulating bacterial toxins. This is a question we are in the process of trying to answer

There may be other ways to poison the capillaries and venules in the way found characteristic of shock. It is not surprising that long anesthesia should be one such, and that the anoxia of hemorrhage should be another. We have searched hard for other toxins at the area of trauma, but we have not found them. In our experiments, fluid loss and infection appear to account for our incidence of shock. From a practical point of view it is good to have it so, for one can act constructively about them because methods for alleviating them both are available.

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RENAL FAILURE SIMULATING ADRENOCORTICAL INSUFFICIENCY*

GEORGE W. THORN, M.D.,† GEORGE F. KOEPF, M.D.,‡ AND MARSHALL CLINTON, JR., M.D.§

BOSTON AND BUFFALO

IT HAS been shown that the hormone of the adrenal cortex aids in the maintenance of a normal state of hydration by increasing the renal tubular reabsorption of sodium, chloride and water.¹⁻⁴ Hence, in the absence of this hormone, as in Addison's disease, excessive sodium, chloride and water are eliminated by the kidneys and, as a consequence, dehydration, hemoconcentration, hypotension and ultimately collapse may ensue. Theoretically, one might expect to encounter at some time a type of renal tubular damage or incapacity that would prevent the adrenocortical hormone from exerting

like state presenting signs and symptoms indistinguishable from those of acute adrenal insufficiency occurring in patients with chronic nephritis and normal adrenal glands has not been reported. The present study is concerned with a report of two patients who, on admission to the hospital, were considered to be suffering from acute adrenal insufficiency. Subsequent studies over a period of two to four years, including post-mortem examinations, proved that the metabolic changes in the body followed renal rather than adrenal disease. These cases are of interest not only because of the

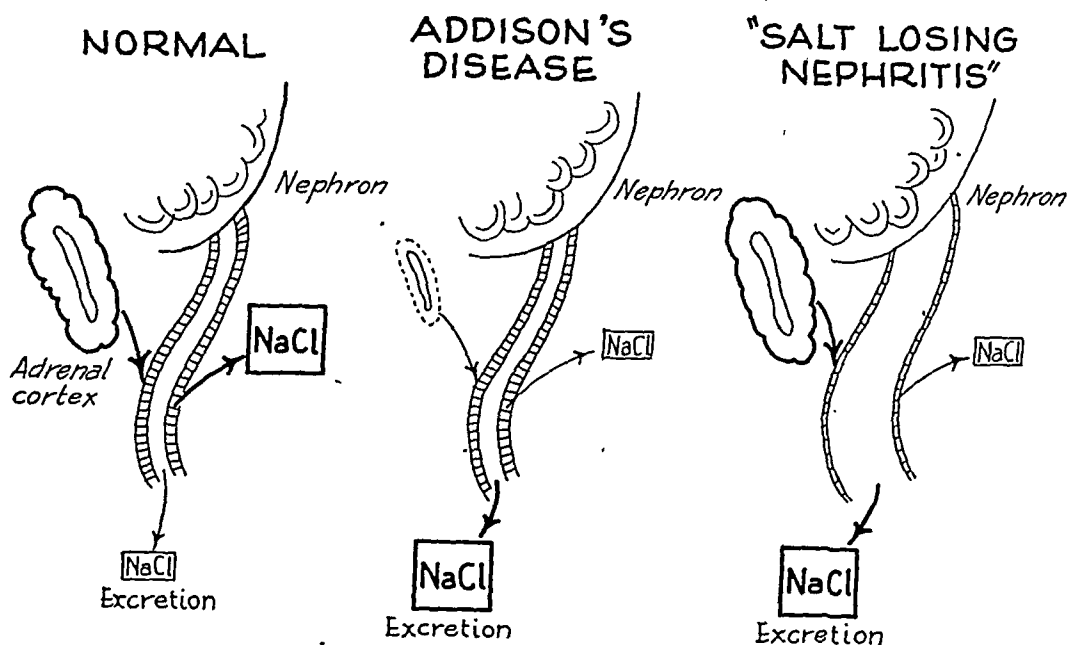


FIGURE 1.

its usual effect on the tubular reabsorption of sodium and chloride (Fig. 1). Under these circumstances a clinical picture simulating the electrolyte disturbance seen in Addison's disease might be presented by a patient with intact, normal adrenal glands.

Hypochloremia and dehydration have been described in patients with renal disease, and the occurrence of this phenomenon in patients with uremia without edema is well known.⁵ To our knowledge, however, the clinical picture of a shock-

physiologic implications that they present but also because therapy directed toward correcting the metabolic disturbances resulted in the rehabilitation of these patients for a life of economic usefulness for periods of two to four years.

OBSERVATIONS

It is of interest to note the close parallelism that occurred in the clinical courses of these patients.

Both were young adults without clinical evidence of previous renal impairment, and both were admitted in a state of collapse with hemoconcentration, dehydration and hypochloremia. Since protein and formed elements were not present in the urine of either patient, both patients were treated initially with sodium, chloride and glucose solutions as well as adrenocortical hormone in an attempt to correct the apparent acute adrenocortical insufficiency.

*From the Department of Medicine, Harvard Medical School, and the Medical Clinic, Peter Bent Brigham Hospital; the Chemical Division, Department of Medicine, Johns Hopkins University and Hospital; and the Department of Medicine, University of Buffalo School of Medicine, and the Medical Clinic, Buffalo General Hospital.

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†Hersey Professor of Theory and Practice of Physic, Harvard Medical School; physician-in-chief, Peter Bent Brigham Hospital.

‡Associate in physiology and instructor in medicine and therapeutics, University of Buffalo School of Medicine; special assistant in medicine and director of metabolic research, Buffalo General Hospital.

§Research fellow in medicine, Harvard Medical School; junior associate in medicine, Peter Bent Brigham Hospital.

Dramatic improvement followed the therapy outlined above. Following restoration of plasma volume and blood pressure, however, azotemia persisted and kidney-function tests revealed marked and persistent high-grade renal insufficiency. Ultimately, it was shown conclusively that, whereas sodium, chloride and water were lifesaving, adrenocortical hormone preparations were of no value in the treatment of these patients. Sustained clinical improvement—for two and a half to four years—accompanied adequate sodium chloride and sodium bicarbonate therapy. Lastly, moderate hypertension, edema and moderate proteinuria developed terminally in both patients.

CASE REPORTS

CASE 1. J. L. (Johns Hopkins Hospital 155764; P. B. B. H. M62361), a 21-year-old man, was admitted to the University of Pennsylvania Hospital on October 18, 1938, complaining of nausea, weakness and vertigo. He had felt well until 1 month prior to admission, when he noted gradually increasing nausea after meals. One week later, he became aware of weakness and vertigo, which was present at first only on exertion but later whenever he was in the erect position. In addition, he had had muscular twitching for several weeks.

At the age of 6 months the patient had a severe throat infection, which was followed by subsequent attacks of less severity. Following tonsillectomy and adenoidectomy at the age of 8, he experienced no further difficulty. There was no history of any other significant childhood illness. His health records at a private school and at a technical school were good. The family history was noncontributory.

During his childhood the patient had noted polyuria and usually had to urinate once during the night. When he was 17 years of age, his appetite became finical. At about that time he found it difficult to arouse himself in the morning because of a sensation of being "doped." In addition, he noted occasional cramps in the legs and feet. A profuse, mucoid postnasal discharge began to manifest itself, and this frequently induced morning nausea and emesis. All these symptoms persisted in varying degree throughout the illness.

Physical examination on admission disclosed a well-developed, freely perspiring young man who appeared chronically ill and evidenced recent weight loss. The blood pressure was 64/46. Generalized sporadic, involuntary, muscular twitchings accompanied by occasional bouts of hiccough were present. The patient was drowsy but aware and intelligent. The skin over the face, body and extremities was markedly freckled, but no abnormal pigmentation was present on the skin or mucous membranes. The axillary and inguinal lymph nodes were slightly enlarged. The ocular fundi appeared entirely normal. There was a uremic odor to the breath. In the right tonsillar fossa a small amount of lymphoid tissue was present. The pharynx was moderately inflamed and a mucoid postnasal discharge was present. The voice was nasal. Examination of the chest revealed no abnormalities. The heart was of normal size, and no murmurs were noted. No abdominal masses or organs could be felt. There was no tenderness in the costovertebral angles. Neurologic examination was not remarkable except for a positive Chvostek's sign.

Laboratory examination at this time disclosed a hemoglobin of 75 per cent and a red-cell count of 4,100,000. Numerous urinalyses disclosed a specific gravity that varied from 1.005 to 1.010. *No albumin or formed elements were present in the urine at any time.* A phenolsulfonphthalein test showed 5 per cent excretion in 2 hours. The blood urea nitrogen was 96 mg. per 100 cc., the serum carbon dioxide combining power 15.0 millimoles per liter, and the chloride 84.8 milliequiv. per liter.

Following the administration of glucose and saline solution intravenously the patient felt greatly improved. Five days later the blood urea nitrogen had fallen to 84 mg. per 100 cc. and the serum chloride had risen to 104.4 milliequiv. per liter. At that time the patient developed a toothache, began to

vomit and experienced pronounced malaise. Chemical determinations following the extraction of a badly infected tooth disclosed a rise in the blood urea nitrogen level to 145 mg. per 100 cc., a fall in the serum carbon dioxide combining power to 12.0 millimoles per liter and a fall in the serum chloride level to 88.7 milliequiv. per liter. Administration of adrenocortical extract intravenously, sodium lactate and glucose solution induced temporary improvement. On November 14, the patient was transferred to the Johns Hopkins Hospital.

Physical examination on admission to this hospital was essentially the same as that reported above except that the blood pressure had increased to 96/54 and the patient appeared less acutely ill. The hemoglobin was 10.8 gm. per 100 cc., the red-cell count 2,000,000, the hematocrit (volume of packed red blood cells) 26 per cent, and the white-cell count 4920, with a normal differential count. The serum nonprotein nitrogen was 112 mg., the total protein 6.0 gm., the blood sugar 86 mg., and the cholesterol 190 mg. per 100 cc. An electrocardiogram was normal. Roentgenographic examination of the heart, lungs, gastrointestinal tract (barium meal) and abdomen (flat plate) disclosed no abnormalities.

The patient was given 30 gm. of sodium chloride (1.5 per cent solution) and 10 cc. of adrenocortical extract intravenously each day. Dramatic subjective and objective improvement followed within 2 days. After 4 days on this regimen the blood nonprotein nitrogen was 63 mg. and the total protein 5.9 gm. per 100 cc., the serum sodium 147.2 milliequiv., the chloride 104.8 milliequiv., the potassium 4.9 milliequiv., the carbon dioxide combining power 24.4 millimoles, and the phosphorus 2.6 millimoles per liter. The urea clearance was 10 per cent of the predicted normal. A phenolsulfonphthalein test showed increased excretion to a total of 15 per cent in 2 hours.

It was impossible to state whether the dramatic improvement that had occurred could be ascribed to the administration of the large doses of sodium chloride, to treatment with adrenocortical hormone or to both. To determine more accurately the agent responsible for improvement, the dose of sodium chloride was reduced from 23 to 3 gm. daily for a 5-day period. Despite the continued administration of adrenocortical extract and 20 mg. daily of desoxycorticosterone acetate (a relatively large dose), the previous symptoms of lassitude, nausea and vomiting returned within 2 days. The blood nonprotein nitrogen rose from 65 to 128 mg. per 100 cc.; the serum sodium fell from 145.6 to 131.0 milliequiv., and the serum chloride from 107.8 to 97.2 milliequiv. per liter. The daily administration of 23 gm. of sodium chloride was reinstituted and was again followed by an alleviation of symptoms and a prompt improvement in the chemical findings. At that time the adrenocortical hormone therapy was discontinued. No relapse occurred, and so far as could be determined the patient did as well on sodium chloride therapy alone as he had on the combination of adrenocortical extract and sodium chloride.

The patient was able to leave the hospital for the Christmas holidays, and during this interval he took 25 gm. of sodium chloride daily by mouth without other therapy. On this regimen he was able to be up and about for 12 to 16 hours a day without excessive fatigue. On January 5, 1939, he was readmitted for further study. The blood pressure was 124/80. During this hospital stay he was maintained in good condition with 25 gm. of supplementary sodium chloride daily. The addition to this regimen of 20 mg. of desoxycorticosterone acetate daily (an excessive dose) for 6 days had little effect on the body weight, plasma volume, serum electrolytes and urinary excretion of sodium and chloride (Figs. 2 and 3), in contrast to the striking effect following the administration of a similar dose to patients with Addison's disease and normal human subjects.⁶ The administration of 2 cc. (200 units) of parathormone was followed by no increase in the urinary excretion of phosphorus (Fig. 4). Furthermore, Pitressin in doses of 0.25 cc. every 4 hours for a 48-hour period failed to reduce the volume of urine significantly and was not accompanied by any gain in body weight (Fig. 5). Studies of the urinary excretion of ammonia indicated extreme limitation of ammonia formation. Since the carbon dioxide combining power of the blood had gradually fallen from 24.4 to 17.2 millimoles per liter, sodium bicarbonate was given by mouth in addition to supplementary sodium chloride.

During the next 2 years the patient was given large doses of enteric-coated sodium chloride tablets (10 to 20 gm. daily) and sodium bicarbonate (5 to 10 gm. daily), administered orally. He felt well, and despite a persistent gradually increasing anemia and a blood level of nonprotein nitrogen ranging from 70 to 130 mg. per 100 cc., he was able to work full time and occasionally to play golf. Episodes of nausea and vomiting, usually occurring in the morning, were relieved by intravenous infusion of sodium chloride solution, which he obtained at his local hospital en route to work. During this period he frequently returned to the Johns Hopkins Hospital for observation. No great change in the clinical status was encountered, except a slight but progressive increase in the degree of anemia. It was also noted that it became increasingly difficult to induce a significant

increased. The heart, which on all previous examinations had been below normal size, was slightly but definitely larger than normal. Urinalysis showed a fixation of specific gravity (1.008) and a + test for albumin. No formed elements were noted. The red-cell count was 1,800,000, the hemoglobin 5.8 gm. per 100 cc., and the hematocrit 24 per cent. The white-cell count was 9300, with a normal differential count. The following chemical findings were noted: nonprotein nitrogen 253 mg., urea nitrogen 187 mg., and total serum protein 5.9 gm. (albumin 3.3 gm.; globulin 2.6 gm.) per 100 cc.; serum sodium, 135 milliequiv., chloride 98 milliequiv., carbon dioxide combining power 20.0 millimoles, calcium 3.9 milliequiv., and phosphorus 4.5 millimoles per liter; and alkaline phosphatase 2.3 Bodansky units per 100 cc. The excretion rate of 17-ketosteroids was 1.6 mg. per 24 hours.

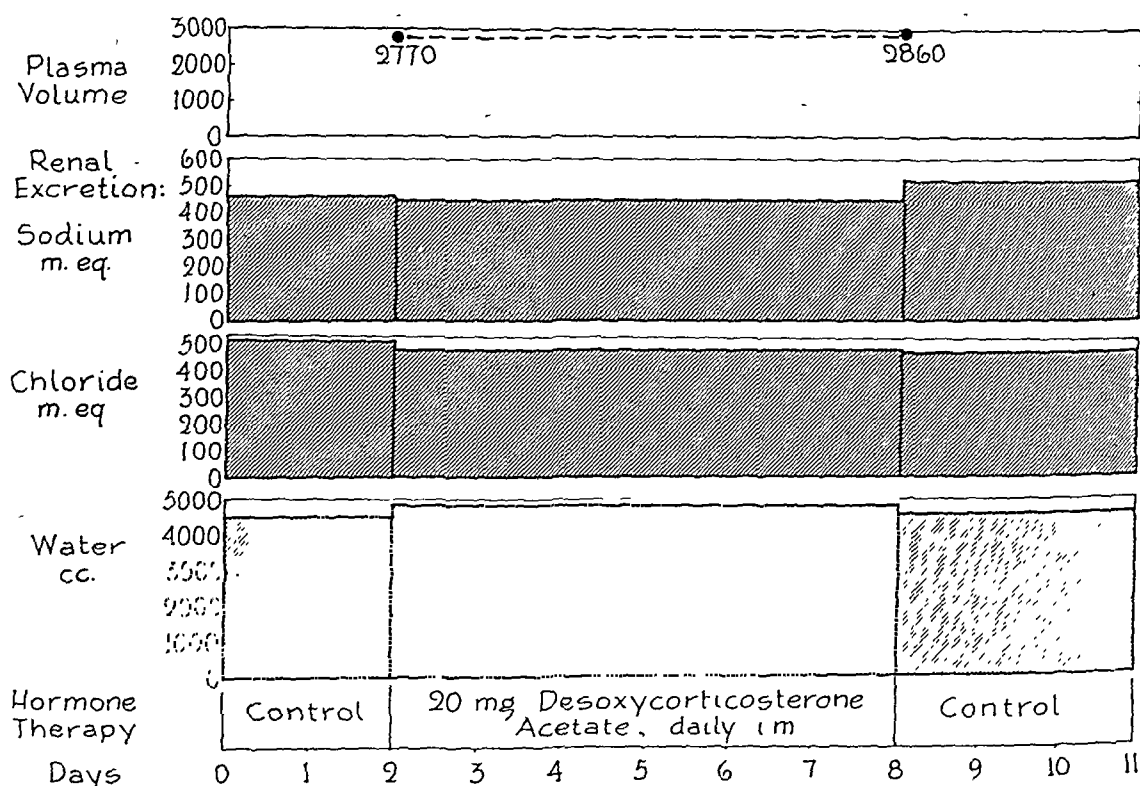


FIGURE 2. Studies on Sodium and Chloride Balance in Severe Renal Insufficiency During Desoxycorticosterone Acetate Therapy (Case 1).

drop in the blood nonprotein nitrogen level by the administration of sodium chloride solution intravenously.

Additional renal-function tests were carried out during this period in an effort to evaluate the clinical situation and to determine the nature of the underlying pathologic process. All tests performed indicated a marked reduction in renal function. Repeated urea-clearance tests gave values ranging from 5 to 15 per cent of normal. The endogenous creatinine clearance averaged 29.5 cc. of plasma per minute, as compared to a normal of 100 to 120 cc. The sulfanilamide clearance was approximately 12 per cent of the expected normal. The tubular reabsorption (T_m) of glucose was 75 mg. per minute, as compared with the normal rate of over 500 mg. Cold-pressor and mental-effort tests disclosed an active, moderately labile vasomotor system.

In April, 1942, the patient while at work crushed his right thumb, which became infected and failed to heal. Within a month weakness and nausea became pronounced. Because of this the patient was admitted to the Peter Bent Brigham Hospital on July 22.

Physical examination at this time differed from the previous examination as follows. The blood pressure was definitely elevated, being 144/90. Edema of the face and extremities was present. The uremic odor of the breath had

Because of the presence of edema and hypertension, it was necessary to reduce the dose of sodium chloride. The patient was placed on a high-carbohydrate, low-protein and low-fat diet and was given 5 gm. of sodium chloride and 2 gm. of sodium bicarbonate daily. He was repeatedly transfused. Despite these measures, the course was one of gradual decline. The mucopurulent postnasal drip increased. The blood pressure fluctuated between 130/80 and 164/95. The white-cell count rose gradually to 33,000. The patient became unable to take any appreciable quantity of nourishment by mouth, so that all medication was administered parenterally. The blood urea nitrogen level gradually rose to 304 mg. per 100 cc.; the serum sodium level fell to 124 milliequiv., and the carbon dioxide combining power to 8.0 millimoles per liter. Twenty-six days after admission, the patient lapsed into coma and died.

Autopsy (Dr. S. Burt Wolbach). The body was that of a normally developed but somewhat poorly nourished young white male who appeared to have had a chronic debilitating disease. The skin was pale and of fair complexion; the hair was red. There were ecchymoses, averaging 1 to 2 cm. in diameter, over both forearms and lower legs. The mouth showed a grayish-brown, granular exudate, with an ulcer 1 cm. in diameter on the buccal cavity opposite the last

olar tooth on the right. There was marked pallor of the mucous membranes and slight cyanosis. Examination of the peritoneal cavity showed the kidneys to be somewhat small on palpation but in their usual position. The bladder was distended to the level of the umbilicus and was estimated to contain 750 cc. of urine, which was pale and rather clear. The pericardial surface was smooth, lustrous and without exudate. The heart was somewhat enlarged and reached to the midclavicular line. The pleural cavity contained 50 cc. of clear amber solution. The surface was grayish red in color, lustrous and without exudate. The heart weighed 400 gm. and was grossly enlarged, most of the enlargement being noted in the left ventricle. The valves were not dilated. The external contour was of the usual conical shape. On the anterior surface of the left ventricle

tures, none of which appeared to communicate with one another. A few submucosal hemorrhages were found in both pelvis. The genital organs were normal. The aorta contained a minimal degree of atheromatous change. The superior vena cava and its tributaries were normal. The trachea was normal; the thymus gland was not identified; the thyroid gland weighed 17 gm.; the parathyroid glands were markedly increased in size, the largest measuring 2 by 1 cm. and the smallest 1.5 by 1 cm. Together the four parathyroid glands weighed 5.7 gm.; they were in their normal location and were grayish yellow. The cut surface revealed a tortuous, smooth parenchyma. The lymph nodes were not remarkable. The bones and bone marrow were normal. No abnormalities of musculature were noted.

Microscopically, the renal architecture was markedly

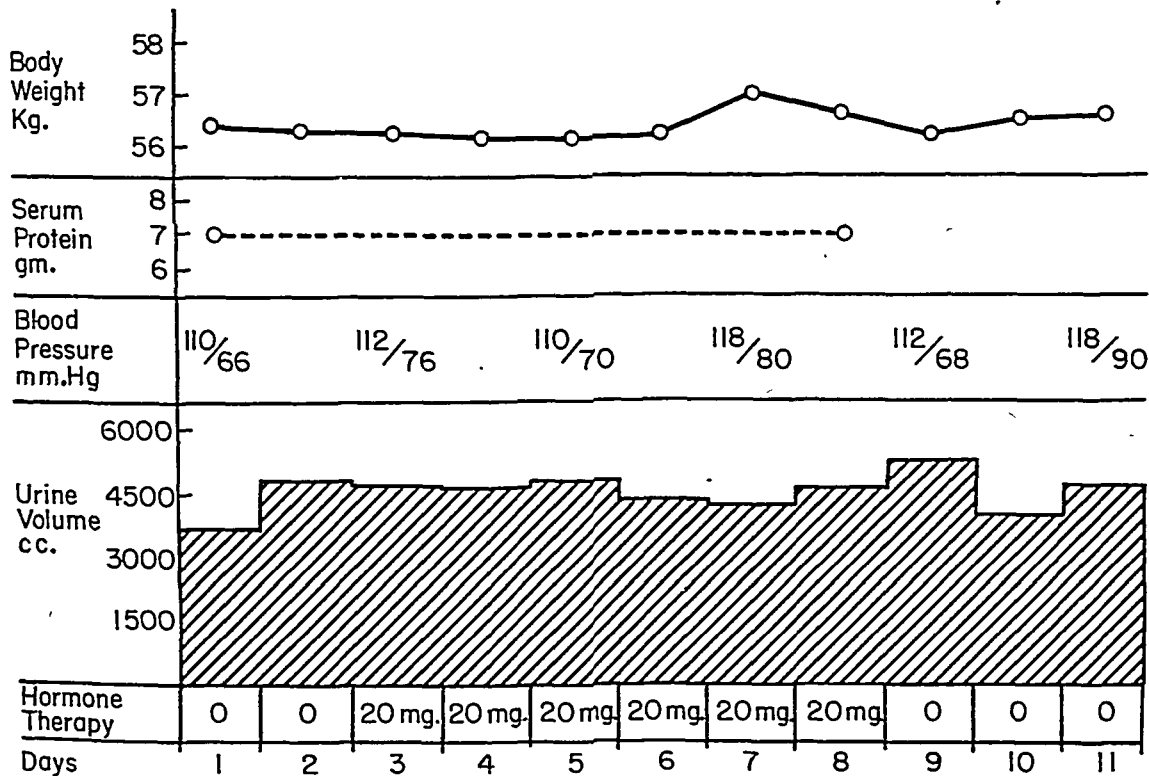


FIGURE 3. Ineffectiveness of Desoxycorticosterone Acetate Therapy in Renal Insufficiency (Case 1).

in the region of the apex there were a few small infiltrations of the myocardium with what appeared to be whitish strands of fibrous tissue. Atheromatous changes of a minimal degree were present in the coronary arteries. The lungs and spleen were not remarkable. The alimentary tract was normal except for a few areas of submucosal hemorrhage, from which no actual bleeding point could be demonstrated. The pancreas weighed 95 gm. and was otherwise normal. The liver weighed 1800 gm. and was normal. The gall bladder and duct were normal. Each kidney weighed 140 gm. No developmental abnormalities of blood vessels or ureters were present. Everywhere over the surface were seen cysts varying from 2 to 40 mm. in diameter. The cyst walls were translucent, and yellowish-colored fluid could be seen within the cysts. The kidney capsule was stripped with difficulty. The external surface of the kidney following stripping was of a mottled gray, white and red tissue being interspersed among the various cysts. This tissue was of a finely and uniformly granular appearance. No gross scars were found. The cysts were present throughout the kidney substances, and among them were irregular strands of parenchyma. In general, the cortex was not more than a few millimeters in thickness, but in a few places measured as much as 6 mm. Tubular striations could not be identified. There was great distortion of architecture everywhere; probably four fifths of the surfaces cut in any direction consisted of cystic struc-

altered by the presence of numerous cystic areas, extensive scarring and extreme dilatation of many of the tubules. There was an irregular increase in the capsular connective tissue. The capsule contained numerous, large, well-filled vascular spaces and in some areas a fair amount of adipose tissue. The inner aspect of the capsule was continuous with the diffuse scarring encountered throughout the renal substance, widely separating the remaining tubules and glomeruli. In many areas it was dense and hyaline, but in others it was fibrillar and appeared to be more recently formed. For the most part, the tubules were lined by low cuboidal or flattened, atrophic epithelium. They were decreased in size and in rare instances contained densely basophilic colloid casts or granular protein material and cellular debris. A striking feature was the separation of the tubules from the capillaries in the scar tissue. Only in a minority of instances did the tubules within the scar tissue closely approximate the capillaries. Many of the latter were well filled with blood elements. Diffusely and irregularly infiltrating the fibrous tissue were moderately large numbers of lymphocytes and plasma cells. Only rare scattered polymorphonuclear leukocytes were present in the interstitial connective tissue.

The glomeruli were decreased in total number in the sections, and those identified showed rather wide variations in size and shape, as well as in the degree of intrinsic glomerular

damage. Throughout the sections were many completely scarred glomeruli, most of which showed scarred adhesions between the fibrosed glomerular tufts and the thickened capsular connective tissue. A fair number of the remaining

capillary tufts were only moderately well filled with blood in most instances.

Throughout all the sections there were large areas in which the tubules showed extraordinary dilatation. These were

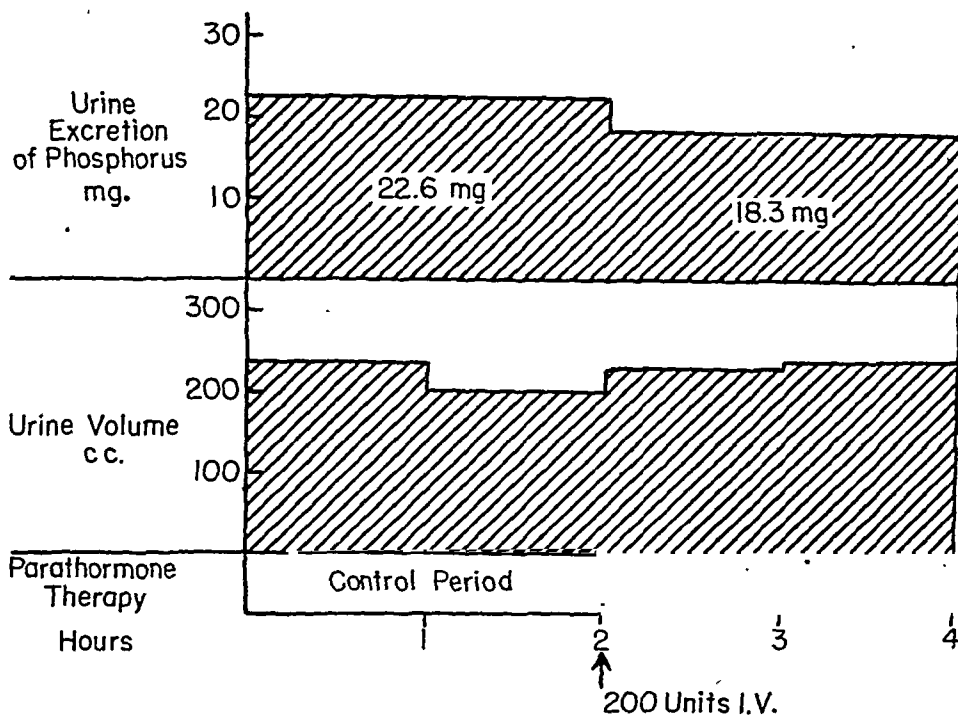


FIGURE 4. Ineffectiveness of Parathormone Therapy in Renal Insufficiency (Case 1).

glomeruli showed evidence of past inflammation. There were adhesions between the glomerular tufts and the capsule, as well as some focal scarring in single capillary tufts. For the most part, the pericapsular connective tissue showed

lined by moderately low columnar or cuboidal epithelium, but for the most part, they were empty or contained finely granular acidophilic protein precipitate. In some instances, adjacent, greatly dilated tubules appeared to be confluent

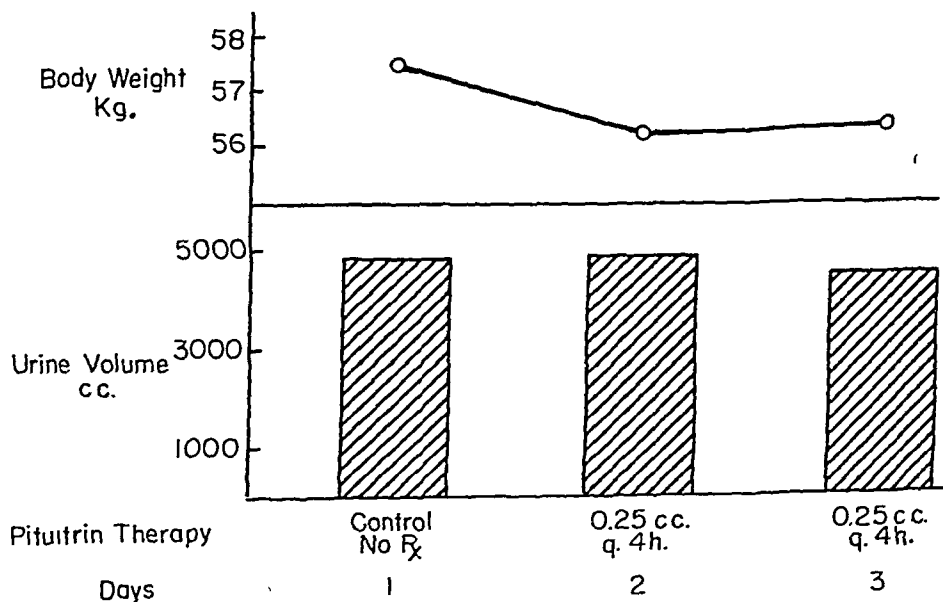


FIGURE 5. Ineffectiveness of Pitressin Therapy in Renal Insufficiency (Case 1).

a diffuse laminar thickness. There was no evidence of an active inflammatory process. Only a few glomeruli were free from adhesions or capsular scarring. The residual

with the formation of irregular cystic areas. Rarely beneath the tubular membrane there were trapped masses of material that had a basophilic staining tendency and suggested cal-

ium deposition. This was accentuated in the sections stained with hematoxylin and eosin. In several areas, both within the tubules and just beneath the tubular epithelium, there were seen masses of refractile, elongated crystals arranged predominantly in a stellate pattern. For the most part, the scar tissue surrounding the greatly dilated tubules was more fibrillar and better vascularized than that surrounding the atrophic tubules previously described.

Also seen throughout the sections were large cystic areas lined by low cuboidal or flattened epithelium and surrounded by scar tissue. These cystic areas were, for the most part, empty, but a few of them contained fine granules of acidophilic precipitated material. These cysts were encountered in the cortex and medullary regions alike, but the greater number appeared to be just beneath the cortex at the juncture of what in a normal kidney would have been cortical and medullary tissue.

The caliceal and pelvic epithelium included in these sections was fragmentary. Beneath this epithelium there was abundant dense connective tissue that had the lymphoid infiltration seen elsewhere in the kidney substance. The arteries and arterioles showed only slight degrees of intimal thickening and hyalinization. Nowhere was there necrotizing arteriolitis or hemorrhage.

The right adrenal gland weighed 16.5 gm. and the left 24 gm. They were of normal consistence. On section, the cut surface of the adrenal cortex was golden yellow. The medulla was pale gray, and some increase in its thickness was present. No cortical adenomas were noted. The left gland was distorted at one pole, where a large spherical nodule was present. On inspection this did not seem to be a neoplasm.

All sections of the parathyroid glands showed an extraordinary degree of hyperplasia. The hyperplastic cells were in clusters and cords that were separated by delicate reticular connective tissue. In many of the cords the cells were heaped up on each other so that no lumens were present. In many instances, however, the cells were arranged around irregular central lumens. In scattered areas throughout all the sections acinous formation was the predominant feature. In one section a few acini were dilated and filled with acidophilic granular substance. The cell composition of the cords or acini varied from area to area. The predominant cells had clear, colorless cytoplasm and distinct cell boundaries and were moderately large. There were numerous interspersed cells with clear or faintly granular acidophilic cytoplasm. The capillaries coursed in the reticular strands of interstitial connective tissue. Most of these were collapsed and poorly filled. In some areas the interstitial connective tissue was increased in amount and hyalinized, and included in these regions were scattered hemosiderin-laden macrophages. A few moderately large vascular channels were well filled with blood cells. Thin trabeculae dividing the hyperplastic glands in roughly lobular architecture appeared to be derived from perivascular connective tissue.

CASE 2. B. P. (Buffalo General Hospital 132264; Johns Hopkins Hospital 230057), a 21-year-old woman, was admitted to the Buffalo General Hospital on February 27, 1940, in coma. She had been in excellent health until August, 1939, when she vomited for the first time. This was followed by repeated attacks of emesis of practically all food ingested. Progressive weight loss and generalized weakness occurred throughout September. The patient felt well during October and November, but in December emesis recurred for 1 week. In February, 1940, the patient again had persistent emesis, became progressively drowsy, and lapsed into coma, at which time she was admitted to the hospital.

The family history was noncontributory. The patient had two siblings who were in excellent health. Her father had a positive serologic reaction but no history, symptoms or physical signs of syphilis.

The patient had had the usual childhood illnesses, but was considered by her parents to have been an unusually healthy child. A tonsillectomy had been performed when she was 12 years old. The blood pressure at that time was normal, and routine preoperative urinalysis revealed no abnormal findings. For 3 or 4 years prior to the onset of her present illness the patient had had nocturia at least once each night. She was the smallest member of her family, and it was thought that she grew less rapidly than her brother and sister. The menstrual history was entirely normal.

Physical examination on admission revealed an acutely ill, emaciated, pale, comatose young woman turning her head from side to side. The rectal temperature was 99°F., the pulse was 120 and weak and thready, and the respirations were shallow and rapid. The blood pressure was 35/0. The skin was dry and the turgor was poor. The eyeballs were soft and the pupils were fully dilated. Examination of the retinal arteries disclosed a slight increase in tortuosity; the fundi were otherwise negative. The chest was clear and resonant. The heart was not enlarged; the rhythm was regular and no murmurs were audible. The heart sounds were distant. The abdomen was soft and no masses were palpable. Pelvic examination revealed no abnormalities. The rectal sphincter tone was good. Knee jerks and ankle jerks were active, and no abnormal reflexes were noted.

Treatment was instituted immediately following admission. Intravenous administration of 5 per cent glucose in physiologic saline solution was begun at once and followed by 1000 cc. of whole blood. The patient was placed in an oxygen tent in the modified Trendelenburg position. The response to this treatment was prompt and dramatic. The blood pressure rose within a few hours to low normal levels and the patient regained consciousness. The following morning (12 hours after admission) she looked and felt greatly improved.

Laboratory examination disclosed a red-cell count of 3,600,000 and a hemoglobin of 7.5 gm. per 100 cc. The white-cell count was 12,350, with a normal differential count. The Kahn and Wassermann reactions were negative. The urine had a specific gravity of 1.010 and a trace of albumin. The chemical findings were as follows: blood sugar 191 mg. per 100 cc.; blood urea nitrogen 249 mg. per 100 cc.; whole-blood chloride 50.8 milliequiv. per liter; serum carbon dioxide combining power 14.1 millimoles per liter, and serum sodium 115 milliequiv., potassium 5.3 milliequiv., calcium 4.1 milliequiv., and phosphorus 6.5 millimoles per liter. The serum albumin was 5.7 gm. and the globulin 1.8 gm. per 100 cc. The whole-blood creatinine was 15.2 mg., the uric acid 8.4 mg., and the cholesterol 156 mg. per 100 cc.

Despite the unusual degree of renal impairment evidenced by the chemical findings, the patient was able to eat fairly well and clinically appeared well. Within 1 week following admission she was up and about the hospital ward. Repeated urinalyses disclosed a fixation of specific gravity at 1.010 and an occasional trace of albumin. *At no time were formed elements present in the urine.* A phenolsulfonphthalein test showed a total excretion of 10 per cent in 2 hours.

Following the administration of liberal amounts of sodium chloride solution the blood urea nitrogen level fell to 195 mg. per 100 cc. and the whole-blood chloride rose to 89.7 milliequiv. per liter. The patient was discharged approximately 3 weeks after admission, feeling reasonably well. At the time of discharge the blood pressure was 100/80.

Following discharge, no specific therapy was given. The patient remained fairly well until May, 1940 (6 weeks later), when she again began to vomit. Emesis occurred in the morning. It became progressively worse and necessitated readmission on June 12. The blood pressure was 106/60, the rectal temperature 99.2°F., the pulse 120, and the respirations 25. The patient was alert. The fundi showed no abnormalities. The remainder of the physical examination was essentially the same as on the previous admission. The outstanding laboratory findings were as follows: red-cell count 3,500,000, and hemoglobin 72 per cent; blood urea nitrogen 264 mg. per 100 cc.; and serum calcium 4.4 milliequiv., serum phosphorus 4.4 millimoles, whole-blood chloride 57.6 milliequiv., serum chloride 71.2 milliequiv., serum sodium 108.7 milliequiv., and serum potassium 4.1 milliequiv. per liter. Repeated urinalyses showed a specific gravity fixed at 1.010, an occasional trace of albumin and *no formed elements.* Roentgenographic examination of the kidney area following the intravenous administration of Diodrast failed to demonstrate the presence of any dye in the renal pelvis.

Immediately following readmission the patient was transfused with 500 cc. of whole blood. Four grams of supplementary sodium chloride was given each day. The intramuscular administration of 5 to 10 mg. of desoxycorticosterone acetate daily for a 2-week period had no significant effect on the renal excretion of chloride. Treatment with 16 gm. of sodium chloride and 5 gm. of sodium bicarbonate daily was then instituted. After 8 days on this regimen the patient developed slight peripheral edema and had several convulsive seizures. Chemical examinations at this time re-

vealed a fall in the blood urea nitrogen level to 42 mg. per 100 cc. and a rise in whole-blood chloride to 94.6 milliequiv. per liter. The plasma carbon dioxide combining power was 7.3 millimoles, the serum calcium 5.0 milliequiv., and the phosphorus 2.7 millimoles per liter; the serum albumin was 2.7 gm., and the globulin 1.9 gm. per 100 cc. Treatment was discontinued for 2 days and the convulsive seizures did not recur. The patient was then given 12 gm. of sodium chloride and 3.6 gm. of sodium bicarbonate daily by mouth, and subjective and objective improvement followed. She was discharged in September.

The patient remained relatively well, aside from occasional bouts of morning nausea and vomiting, and was able to do part-time work. Her nausea was controlled by the intravenous administration of physiologic sodium chloride solution. In addition, frequent blood transfusions were given in an effort to correct the anemia. Medication was gradually increased to 15 gm. of sodium chloride and 6 gm. of sodium bicarbonate daily. During that period the blood urea nitrogen level ranged between 73 and 111 mg. per 100 cc. In May, 1941, the patient was admitted to the Johns Hopkins Hospital for further study.

Physical examination on admission disclosed a moderately well-nourished, somewhat underdeveloped young woman. The blood pressure was 128/80. No abnormal skin or mucous membrane pigmentation was noted. The retinal vessels were moderately tortuous, with more than normal shimmer to the retina. The thyroid gland was palpable. The heart was not enlarged. A low-pitched systolic bruit was present over the precordium. The kidneys were not palpable. The extremities were not remarkable. No edema was present. The deep tendon reflexes were hyperactive; there was no Chvostek's sign.

Urinalysis showed a clear urine with a specific gravity of 1.010 and a trace of albumin but no formed elements. The red-cell count was 2,700,000, the hemoglobin 8 gm. per 100 cc., the hematocrit 24.1 per cent, and the white-cell count 6400, with a normal differential count. The following chemical findings were noted: nonprotein nitrogen 150 mg., blood urea nitrogen 110 mg., blood sugar 96 mg. and serum protein 7.3 gm. (albumin 5.3 gm. and globulin 2.0 gm.) per 100 cc.; and serum chloride 95.4 milliequiv., the carbon dioxide combining power 21.2 millimoles, potassium 8.6 milliequiv., calcium 4.0 milliequiv., and phosphorus 3.6 millimoles per liter.

Radiographic examination showed the heart to be small and the lungs clear. The long bones appeared normal, but a minimal amount of calcification in the vessels of the lower legs and feet was noted. The kidneys were visualized on a flat plate of the abdomen and appeared small. The electrocardiogram was normal. Various tests of renal function were performed in an effort to elucidate further the nature of the underlying pathologic process. All these tests indicated a high degree of renal failure. The urea clearance was approximately 4 per cent of normal. A phenolsulfonphthalein test showed a total excretion of 9 per cent in 2 hours. The endogenous creatinine clearance was likewise greatly reduced (5.3 cc. per minute per square meter of surface area), and the tubular reabsorption (T_m) of glucose was also markedly impaired. The patient was discharged on May 28. At that time she was taking 12 gm. of supplementary sodium chloride and 6 gm. of sodium bicarbonate daily.

During the remainder of the year, the patient was followed in the Out-Patient Department of the Buffalo General Hospital. She remained moderately well and was able to lead a fairly active life, although occasional bouts of morning nausea and emesis continued to occur. During this period she continued to receive large doses of supplementary sodium chloride medication, which were necessary to allay nausea and to prevent a gradual rise in the blood nonprotein nitrogen level. As time went on, the quantity of sodium chloride solution that induced edema and convulsions became appreciably smaller, so that it became increasingly difficult to maintain the supplementary sodium chloride intake at a level that would alleviate nausea and keep the blood nonprotein nitrogen level from rising.

In January, 1942, the blood pressure had increased to 158/96. The blood urea nitrogen was 130 mg. per 100 cc., the serum chloride 116 milliequiv., the calcium 3.7 milliequiv., the phosphorus 3.0 millimoles and the carbon dioxide combining power 18.5 millimoles per liter, and the total protein

was 23.6 Bodansky units per 100 cc.

A few weeks later the patient complained of some diminution of visual acuity. Marked edema and punctate hemorrhages were noted in both retinas. The blood pressure had increased to 160/120. The heart was definitely enlarged, and ankle edema was present. Despite a reduction in the dosage of sodium chloride, the edema continued to increase and involved the face and abdominal wall as well as the legs and ankles. The patient was readmitted to the Buffalo General Hospital because of these findings. Despite all measures, her course progressed gradually downhill. Nausea and emesis were more frequent. On March 29, generalized convulsions began. At that time the blood pressure was 180/140, the blood urea nitrogen 144 mg. per 100 cc., and the serum chloride 100.5 milliequiv., the calcium 2.7 milliequiv. and the phosphorus 3.9 millimoles per liter. Following the convulsions, crepitus and swelling were noted over both clavicles. The presence of fractures was confirmed radiographically. Despite the administration of sedatives in large dosage, severe generalized convulsions recurred each day until April 4, when the patient's temperature rose to 107°F. and she expired.

Autopsy (Dr. Kornell Terplan). The body was that of a 154-cm.-long young woman. The entire integument showed a peculiar yellowish-gray coloring. There was distinct edema of the labia majora. The extremities showed slight edema, especially around the ankles. There was also slight edema of both upper arms. The breasts were extremely small and contained little parenchyma. The fat tissue of the breast showed distinct edema. The lower lip was edematous and slightly cyanotic. The teeth were in good condition, as inspected from without, and the gingiva was slightly bluish. The hair was light blond and fairly abundant. The pupils were 5.6 mm. in diameter.

The kidneys appeared markedly shrunken. The right kidney weighed 60 gm. and measured 9 by 3.5 by 3 cm.; the left kidney weighed 42 gm. and measured 7.5 by 3.5 by 2 cm. The capsules were unusually firmly adherent to the cortex. The capsule of the right kidney appeared somewhat thicker than that of the left. On the cut surface, a completely obscured picture was seen. The normal markings had disappeared. The cortex and medulla practically blended into one another, but even so it was apparent that the cortex was markedly atrophic, averaging between 1 and 2.5 mm. in thickness. The color of the cut surface was yellowish pink. No hemorrhages were visible grossly. After the capsule had been removed with great difficulty, the surface had a fairly regular, fine granular appearance, and here and there somewhat yellowish areas were noted near the surface. A few lentil-sized cysts and one hazelnut-sized cyst were present in the right kidney. The left kidney showed exactly the same picture. The fat tissue in the hilus of the kidney appeared relatively increased in amount. The kidney pelvis on each side was of corresponding dimensions. In the right pelvis, there were recent hemorrhages in the mucosa. The gross picture of the kidney was that of diffuse uniform shrinkage corresponding most closely to the late stages of contraction seen in diffuse glomerulonephritis. The branches of the renal arteries were not noticeable, and on section were apparently not thickened or stiffened. The right kidney was duplex, with two renal arteries, which were of normal caliber.

The adrenal glands were of normal size and weighed 7.5 and 8.5 gm. There was considerable lipid in the cortex. In one gland there were recent capillary hemorrhages in the medulla.

The heart weighed 270 gm. and showed distinct hypertrophy of the left ventricle, which measured 2 cm. in thickness near the bases. The right ventricle measured 5 mm. in the pulmonary conus. The trabeculae of the right side of the heart were fairly prominent. The endocardium in the left atrium showed moderate fibrosis. About 50 cc. of fluid was present in the pericardial sac. The thoracic duct was not remarkable. The foramen ovale was closed. The mitral ostium measured 8.5 cm. in circumference. The aortic valve measured 6 cm. in circumference, the pulmonary valve, 6.5 cm., and the tricuspid, 11 cm. The myocardium was slightly yellowish gray, apparently owing to a slight degree of anemia.

Both lungs showed moderate passive hyperemia and edema. There were fairly diffuse suffusions in the visceral pleura. The parenchyma in both lobes was decidedly consolidated

and dark bluish red. The trachea and bronchi showed marked hyperemia and capillary hemorrhages in the mucosa. The tracheobronchial lymph nodes were small and anthracotic. About 100 cc. of slightly bloody fluid was present in each pleural cavity. Both lower lobes showed superficial atelectasis, especially at the posterior aspects. The thyroid gland was of normal size. The cervical lymph nodes appeared moderately hyperemic. Three parathyroid glands were identified, one of them being slightly larger than normal. The larynx was not remarkable. The thymus gland was present but was considerably reduced in size.

The liver was normal in size and showed distinct passive congestion, edema and slight fatty changes of the peripheral portions. The bile ducts and gall bladder were not remarkable. The gall bladder was thin walled and not edematous and contained yellowish bile. The stomach showed a few coffee-groundlike flecks but no recent hemorrhages. The spleen was of normal size and contained a lentil-sized phlebotomy. The pancreas was not remarkable. The entire small intestine showed a peculiar greenish-black discoloration of the mucosa and contained somewhat digested semifluid matter. No hemorrhages were seen grossly. The mesenteric lymph nodes were small, and the colon showed a few petechial hemorrhages near the cecum. There was considerable pseudomelanosis throughout the mucosa of the small intestine. The thoracic and abdominal aorta were not remarkable.

The ribs were thin and cut easily. The cortex appeared somewhat atrophic. The bone marrow was distinctly reduced, and that in the vertebral bodies appeared somewhat anemic.

A variety of sections of the kidneys taken in vertical and frontal planes through the cortex and medulla showed the same picture of marked contraction, with almost all the glomeruli completely or almost completely hyalinized. Considerable hyalinization atrophy of many tubules with practically complete obliteration of their lumens was also noted. The few glomeruli still present were hypertrophic. They showed synchias to the capsule and, here and there, glandlike proliferation of the capsule epithelium. There were rare crescents, but these were for the most part hyalinized. A few glomeruli showed recent dilatation of capillaries, some of them with a considerable accumulation of leukocytes. Some had older hyaline and leukocytic exudate in the capsular space in the process of organization. A few recent capillary thrombi consisting mostly of fibrin and red blood cells were noted. The proximal convolutions were for the most part distended. They showed considerable epithelial desquamation and some fatty droplets. Here and there, erythrocytic, granular and a few small leukocytic casts were noted. The interstitial tissue showed dense infiltration with lymphocytes. The capsule was markedly thickened, infiltrated by lymphocytes and firmly adherent to the kidney. The branches of the renal artery showed only slight thickening of the intima. There was distinct thickening of arteries and arterioles only in the entirely fibrotic areas. In the remainder of the kidney the walls of the small arteries and arterioles were not remarkable. The entire picture corresponded to diffuse glomerulonephritis in the final state, with considerable fibrotic atrophy but still with marked degenerative changes in the somewhat hypertrophic proximal convolutions.

In the parathyroid glands, simple hyperplasia and marked hyperemia were observed. All the cells were so-called "water-clear" cells. Distinct edema was present in the capsules. All sections showed extensive ectasia of capillaries. One parathyroid gland contained a few minute follicles filled with colloid.

The clinical course of these patients is summarized in Tables 1 and 2. The onset of the disease, the clinical and laboratory findings, the response to therapy and the subsequent course of the disease were closely similar in both cases. Both patients were young adults (twenty-one years of age) on admission. The past history in both cases revealed little of significance except long-standing nocturia. There was no history of previous renal disease. The absence of abnormal skin or mucous-membrane pigmentation and the spontaneous hypoglycemia

were noteworthy. Routine urinalysis revealed only a slight trace of albumin. No formed elements were present in the urine sediment. Chemical examination of the blood revealed a striking reduction in the serum chloride level and an unusually high nonprotein nitrogen level. The hypotension, the small size of the heart, the absence of vascular changes in the retinal vessels and the essentially normal urine, however, favored a diagnosis of Addison's disease rather than that of uremia secondary to chronic nephritis.

Administration of adrenocortical hormone parenterally, sodium chloride solution intravenously and transfusion was followed by dramatic improvement in both patients. The blood pressure rose to normal levels within twelve hours, and nausea and vomiting ceased. Administration of sodium chloride solution and adrenocortical hormone was continued each day; despite the alleviation of symptoms and the restoration of normal blood pressure and serum chloride levels following this therapy, it was noted that the blood urea nitrogen failed to return to normal. Furthermore, phenolsulfonphthalein excretion was found to be reduced to less than 10 per cent of dye in two hours. These findings, although indicative of high-grade renal failure, did not eliminate the possibility of coexistent adrenal failure. Because of the critical condition of these patients, it was not considered justifiable to discontinue adrenocortical hormone therapy. It was found that both patients were able to tolerate 12 to 15 gm. of sodium chloride and 5 to 6 gm. of sodium bicarbonate daily without developing edema or hypertension, and that on this regimen the serum sodium and chloride concentrations were maintained at normal levels, the blood urea nitrogen level was reduced from 120 to 70 mg. per 100 cc., and both patients were able to lead a life of normal activity. Subsequently, carefully controlled studies revealed that the administration of desoxycorticosterone acetate (synthetic adrenocortical hormone) in large amounts was ineffective in maintaining sodium and chloride balance.

In Case 2, the patient discontinued sodium chloride administration following her initial discharge from the hospital. During the next two months weakness, nausea and vomiting recurred. These changes were associated with a fall in the blood pressure and the serum chloride level (to 71.2 milliequiv. per liter) and a rise in the blood urea nitrogen level (to 264 mg. per 100 cc.). Restitution of supplementary sodium chloride therapy was followed by a prompt remission in symptoms and marked improvement in blood pressure and blood chemistry.

Extensive renal-function tests were performed on both patients in an effort to determine whether the renal lesion primarily represented extreme reduction in all functional elements of the kidney or a specific defect in tubular reabsorption of sodium and

chloride. For details of these tests the reader is referred to the protocols. All tests performed indicated an extreme reduction in functioning renal mass. The degree of renal failure was so great that a valid comparison of the possible differences between glomerular filtration and tubular reabsorption could not be made.

In addition to renal-function tests, experiments were carried out to determine the effect of the ad-

The most striking feature presented by these patients was their ability to tolerate large quantities of sodium chloride (10 to 15 gm. daily) and sodium bicarbonate (4 to 6 gm. daily) without the development of edema and hypertension, in the presence of high-grade renal insufficiency. This phenomenon persisted until one to two months prior to death. It appeared that the ability of the kidneys to reabsorb sodium chloride in excess of

TABLE 1. *Summary of Data in Case 1.*

DATE	BLOOD PRESSURE	BLOOD UREA NITROGEN	THERAPY		BODY WEIGHT	EDEMA	PHENOLSULFON- PHTHALEIN EXCRETION
			SODIUM CHLORIDE	SODIUM BICARBONATE			
	<i>mm.Hg.</i>	<i>mg./100cc.</i>	<i>gm.</i>	<i>gm.</i>	<i>kg.</i>		<i>%</i>
1938: Oct.	64/46	132	*	*		0	5
Nov.	92/68	94	12	0	56	0	15
1939: Jan.	112/80		15	5	58	0	15
Oct.	96/50	129	12	6	55	0	5
1940: Sept.	128/78	109	12	6	56	0	
1941: May	120/70	102	12	6	58	0	9
1942: Feb.	134/90		10	8	57	+	
Aug.	145/90	304	*	*	52	++	

*Intravenous therapy consisting of glucose, sodium chloride and sodium lactate solutions.

ministration of hormones whose action is known to be primarily or largely on the renal tubules. The inability of desoxycorticosterone acetate, parathormone and pituitrin treatment to affect the renal excretion of sodium chloride, phosphorus and water, respectively, is demonstrated in Figures 2, 3, 4 and 5. Administration of 20 mg. of desoxycorticosterone acetate daily for six days produced no significant change in the plasma volume or electrolyte balance

water was greatly impaired in both patients, and that the administration of large doses of supplementary sodium chloride was therefore necessary for the maintenance of an adequate plasma volume. Such treatment presented further increase in the level of blood urea nitrogen.

Both patients showed decidedly elevated serum phosphorus levels on all examinations. The serum calcium levels, however, were normal in one pa-

TABLE 2. *Summary of Data in Case 2.*

DATE	BLOOD PRESSURE	BLOOD UREA NITROGEN	THERAPY		BODY WEIGHT	EDEMA	PHENOLSULFON- PHTHALEIN EXCRETION
			SODIUM CHLORIDE	SODIUM BICARBONATE			
	<i>mm.Hg.</i>	<i>mg./100cc.</i>	<i>gm.</i>	<i>gm.</i>	<i>kg.</i>		<i>%</i>
1940: Feb.	30/0	249	*	0	36	0	5
Mar.	98/76	127	6	0	37	0	
June	104/62	264	15	5	36	0	5
Sept.	144/92	97	15	5	44	0	
Dec.	128/84	67	16	6	42	0	
1941: June	128/80	102	12	5	42	0	9
1942: Jan.	154/100	76	20	4	42	++	
Apr.	138/100	148	*	*	43	++	

*Intravenous therapy consisting of glucose, sodium chloride and sodium lactate solutions.

(Figs. 2 and 3), whereas in normal subjects a striking increase in plasma volume and retention of sodium and chloride was encountered following the administration of 10 mg. of desoxycorticosterone daily.⁶ Administration of 200 units of parathormone (Fig. 4) failed to evoke the phosphorus diuresis induced by this hormone in normal subjects.⁷ Administration of pitressin (0.25 cc. every four hours) failed to effect a reduction in urine volume (Fig. 5). It is evident from these findings that failure to reabsorb sodium and chloride was not a specific metabolic defect on the part of the renal tubules of these patients. Glycosuria was not observed at any time.

tient (Case 1) and definitely below normal in the other (Case 2). It is of interest that latent tetany was usually present in the latter but less frequently so in the former. Involuntary muscular twitchings on the other hand, were seldom observed in Case 2 but were prominent in Case 1.

In Case 1, the patient was maintained in relatively good clinical condition for a period of nearly four years, and in Case 2 for slightly over two years, by the administration of large doses of supplementary sodium chloride and sodium bicarbonate. The terminal course in the two patients was similar. In each case it was noted that it gradually became increasingly difficult to maintain the sodium

chloride intake at a level that would prevent a rise in the blood urea nitrogen level and alleviate nausea and vomiting and yet not lead to hypertension and edema. At the same time, definite vascular changes began to appear in the vessels of the ocular fundi. Terminally, both patients lost ability to tolerate large doses of sodium chloride and developed edema, moderate hypertension and increasing nitrogen retention. The clinical picture changed considerably, so that at death it was perfectly consistent with the usual findings in long-standing chronic nephritis. The immediate cause of death was cardiac failure in Case 1, and uremic convulsions in Case 2.

DISCUSSION

It is our belief that the clinical syndrome that has been described is probably not associated with a typical pathologic lesion in the kidney, but rather occurs late in the course of insidious, slow but progressive renal disease. The slow rate at which the disease progresses and the absence of involvement of all nephrons at any one time permit considerable adaptation to fairly high-grade renal insufficiency. There result extensive scarring, hypertrophy of remaining glomeruli and dilatation of tubules. Under these circumstances the nice balance that normally exists between the quantity of sodium and chloride filtered through the glomeruli and reabsorbed by the tubules is disturbed to the extent that a small excess of sodium chloride is lost daily; ultimately this results in severe depletion of extracellular fluid volume, hemoconcentration and finally increasing renal failure. Increased water intake, without sodium chloride, accentuates the deficiency by increasing urine volume and hence sodium chloride loss.⁸ Terminally, with loss or impairment of the few remaining nephrons, the kidney is further limited in its function and both salt and water are retained, resulting in edema, hypertension and cardiac failure. It is our impression that ordinarily few patients live long enough in this precarious balance to reach the stage of severe dehydration and circulatory collapse. A moderate grade of sodium chloride depletion is not infrequently observed in patients with chronic nephritis, particularly when renal impairment is due to healed pyelonephritis, hydronephrosis or vascular nephritis (Peters⁵). It is possible to rehabilitate a number of these patients for periods of months to years by the careful administration of supplementary sodium chloride (1 to 5 gm. daily) and sodium bicarbonate (1 to 5 gm. daily) in conjunction with a large fluid intake (2500 to 4000 cc. daily). The administration of water alone, if it gives rise to a diuresis, may result rather rapidly in sodium and chloride depletion and hence ultimately reduce the volume of extracellular fluid and blood plasma and induce further renal insufficiency.⁸ The sodium chloride and sodium bicarbonate must be administered cautiously, in small doses and with due regard for the state of the circulation. Only those patients

with adequate cardiac reserve can derive benefit from increasing plasma volume and hence glomerular filtration with sodium chloride and sodium bicarbonate administration. Impending heart failure and excessive hypertension are contraindications to supplementary sodium chloride therapy, even in uremia.

Throughout the present paper merely the level of blood urea nitrogen has been discussed. This has not been done with the idea that the elevated blood urea is necessarily responsible for the clinical symptoms observed in uremia, but rather because in most cases the blood urea level parallels the clinical state.

SUMMARY AND CONCLUSIONS

A syndrome characterized by excessive loss of sodium, chloride and water, resulting in collapse and associated with renal disease rather than adrenal disease, is described.

Adrenocortical hormone is of no value in correcting the mineral depletion of these patients, since the renal tubular cell on which the hormone normally exerts its effect is unable to respond to additional hormone.

At present there does not appear to be a specific pathologic change responsible for excessive sodium and chloride loss other than widespread renal damage, associated with extensive scarring, a few remaining hypertrophied glomeruli and dilated tubules. Less severe loss of sodium and chloride is not infrequently observed in patients with chronic nephritis, and striking benefit may follow the judicious use of small quantities of supplementary sodium chloride and sodium bicarbonate under these circumstances.

For convenience and for its therapeutic implication, patients with chronic renal disease presenting evident signs and symptoms of sodium and chloride depletion may be said to be suffering from "salt-losing nephritis."

We are indebted to Drs. Richard A. Kern and Francis D. W. Lukens, of the University of Philadelphia, for their kindness in referring Case 1, and to Drs. Clayton W. Greene and Abraham H. Aaron, of the Buffalo General Hospital, for referring Case 2.

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THE PROBLEM OF TUBERCULOSIS CONTROL*

JOHN A. FOLEY, M.D.,† AND JOHN B. ANDOSCA, M.D.‡

BOSTON

THE tuberculosis-control problem must be considered as the all-important factor if there is to be a reduction in the mortality and morbidity rate from pulmonary tuberculosis. One is told time and again that pulmonary tuberculosis is becoming a disease of the past and that it is only a matter of several years before it will be entirely eradicated. This is certainly a false notion. To be sure, the death rate in the United States has dropped from 201 per 100,000 in 1900 to 43 in 1940, but it must be remembered that this disease is still the leading cause of death between the ages of twenty and forty. The public is not aware of the magnitude of the present tuberculosis problem. This apparent indifference regarding tuberculosis is shown by the man in the street, who believes, in the absence of tuberculosis in his family, that the problem is non-existent.

It is apparent from a review of the death rate by occupation, age and sex that the largest numbers of

cases returned to society is small. In other words at present these huge sums of money are being spent yearly for the care and treatment of patients whose disease in 90 per cent of the cases is advanced. It would be a sound investment if more funds could be available for the maintenance of a sound and efficient tuberculosis-control program. By such a program the number of minimal cases would be definitely increased, and at the same time there would be a corresponding decrease in advanced cases.

At the Boston Sanatorium, the number of minimal cases admitted is certainly small (Table 1). It has also been noted that the female patients admitted fall into a lower age group than do the male patients. As would be expected, the age at death in the male patients is higher than that in the female patients (Fig. 1).

Although health departments are usually charged with the responsibility of city tuberculosis control

TABLE 1. Stage of Disease on Admission.

STAGE	1936	1937	1938	1939	1940	1941	1942
Minimal	78 (15%)	55 (10%)	52 (9%)	49 (10%)	46 (8%)	43 (7%)	73 (11%)
Moderately advanced.....	129	133	165	231	264	394	412
Far advanced	285	314	305	227	241	178	175
Totals	492	502	522	507	511	615	660

tuberculosis patients are to be found among the underprivileged and low-salaried groups. The huge economic and financial burden of the disease can easily be realized when the cost of long hospitalization is taken into consideration. The taxpayer supports this huge bill, and it is only a matter of time before he will ask for an accounting of these expenditures. That the tuberculosis sanatorium has contributed to the decline in tuberculosis cannot be denied. This contribution can be attributed more to the segregation of positive-sputum cases than to the number of arrested cases. The tuberculosis sanatorium could not possibly justify the expenditure of millions of dollars of the taxpayers' money on the basis of returns to the community in the form of arrested cases.

When it is considered that 90 per cent of the patients admitted to the sanatoriums have advanced disease, it is no wonder that the number of arrested

the sanatorium by virtue of its personnel and equipment should assume a place in the control program. The health department and the sanatorium should work as a single team, hand in hand, to assure success of any tuberculosis-control program. The City of Boston is fortunate in having an efficient health department that is properly and scientifically equipped and conducted. Through its able physicians and public-health nurses, together with its practicing physicians, it is safe to predict that there will be an increase in the number of minimal cases. The participation of the practicing physician is extremely important to a chest-clinic program, especially in the early notification of all cases of pulmonary tuberculosis. In this regard, it should be pointed out that in 1942 there were 388 deaths from pulmonary tuberculosis in Boston, yet only 209 of these occurred in the Boston Sanatorium. The remaining 179 patients must have died either in one of the general hospitals or at home. It is certain that the number that died in general hospitals is very small. It may be added that of the 209 deaths in the sanatorium in 1942, 57 per cent occurred within six months after the patients' admission (Table 2).

*From the Boston Sanatorium and the Department of Medicine, Boston University School of Medicine.

†Chief of staff, Boston Sanatorium; clinical professor of medicine, Boston University School of Medicine; director of Fifth and Sixth Medical Services, Boston City Hospital.

‡Chief resident physician, Boston Sanatorium; instructor in medicine, Boston University School of Medicine.

It is unfortunate to see time and again the notation of a case of tuberculosis and the death cer-

TABLE 2. Length of Stay in Sanatorium of 209 Patients Who Died in 1942.

PERIOD	NO. OF PATIENTS	PERCENTAGE
3 mo.	94	44
6 mo.	27	13
12 mo.	33	16
over 1 yr.	55	26

ificate dated within one or two days of each other. It is obvious that there is an urgent need for more

sanatorium against advice. A patient of this type is a source of danger not only to himself but also to his family and the community. Many of these patients go to and from the sanatorium at will, with the result that there has been a definite increase in readmissions (Table 4). The State legislators should look into this all-important problem in dealing with the unco-operative tuberculosis patient. Health laws should be strictly enforced in segregating this type of patient.

At the Boston Sanatorium during the last six

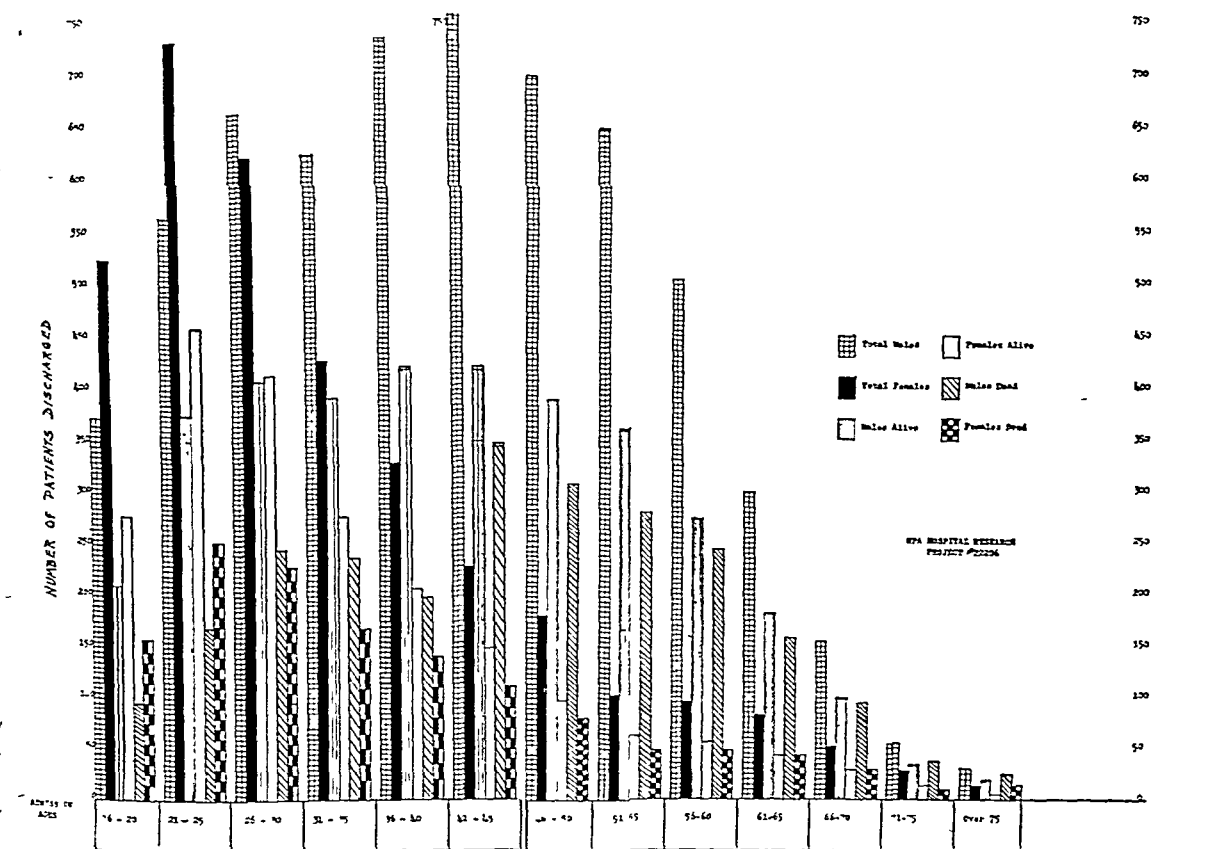


FIGURE 1. Age Distribution of Patients with Pulmonary Tuberculosis Who Were Admitted to the Boston Sanatorium from 1920 to 1942, inclusive.

progressive, energetic case finding and early notification.

It is important to note that the number of patients discharged as apparently arrested, arrested or

years there has been an increase in the number of patients admitted, treated and discharged, whereas the average stay of the patient has been reduced (Table 4).

A considerable sum of money should be allotted in educating the public in the problem of tuberculosis.

TABLE 3. Condition of Patients on Discharge.

	1936	1937	1938	1939	1940	1941	1942
Arrested or quiescent ..	122	202	199	225	172	171	223
Improved ..	164	112	142	130	163	214	249
Unimproved ..	13	19	31	24	35	29	41
Non-tuberculous ..	7	6	11	15	15	12	7
Deaths ..	190	196	170	134	197	168	209
Totals ..	496	535	553	528	582	594	729

quiescent is small as compared to the number who are discharged as improved and unimproved, with, in most cases, a positive sputum (Table 3).

It is a waste of public funds to treat a patient for a few months or weeks and have him leave the

TABLE 4. Additional Data.

	1936	1937	1938	1939	1940	1941	1942
Total patients treated ..	1079	1088	1082	1042	1070	1110	1160
Readmissions ..	105	87	127	143	176	158	234
Average stay (in days) ..	411	426	434	400	352	304	312
Mortality (per cent) ..	17.5	18.0	15.7	12.8	18.4	15.1	17.7

The public is made somewhat tuberculosis-conscious by the sale of Christmas Seal stamps. The local medical societies should bring the tuberculosis

problem before the public even if it entails employing the radio and cinema.

All high-school children should be given the Mantoux test, and roentgenograms should be taken of all those with a positive reaction. Motorized x-ray field units, each accompanied by a trained roentgenologist and a technician, should be sent into those parts of the city from which most of the cases of tuberculosis come. The Army has aptly shown what can be done by mass x-ray examination. All inductees are examined by means of the 4-by-5-inch photoroentgenogram. It is said that about 1 per cent of all the inductees thus examined were found to have pulmonary tuberculosis. Of these, 90 per cent were found to be in the minimal stage of the disease, and approximately 10 per cent of the cases were classified as advanced. This figure corresponds closely, in reverse ratio, to the minimal and advanced cases admitted to this sanatorium. Many of the larger industrial firms are employing mass x-ray examination of their employees, with profitable results.

A geographic study of the entire city should be undertaken, for it can safely be said that most of the patients in the sanatorium come from certain sections, such as the crowded districts in Charlestown, East Boston, the South End and the North End.

Food handlers should be more carefully checked. It is surprising to see the number of patients admitted to the sanatorium who have been employed as cooks and waitresses.

In addition to the early diagnosis and treatment of pulmonary tuberculosis, it is important to secure the education and rehabilitation of the patient so that he may resume his rightful place in society. This education should be begun as soon as he is admitted to the sanatorium. The adjustment of the patient to his new environment and the solution of his family and economic problems are essential for ensuring a speedy and safe recovery.

Physicians and health units must be taught that post-sanatorium care is just as important as sanatorium care. There is no doubt that the patient will find himself back in the sanatorium unless post-sanatorium care is carefully carried out. It is the duty and obligation of the community to see to it that the patient and his family are well provided for. By so doing the community will realize a profitable return on the investment that has been made.

* * *

In summary, even if it is not possible at present to eradicate pulmonary tuberculosis, owing to its multiple and complex aspects, at least a well-managed and efficient program of tuberculosis control can and should be employed. This will surely bring about a definite reduction in the economic burden, mortality and morbidity rate resulting from pulmonary tuberculosis.

We are indebted to the W.P.A. Hospital Project 22206 for the preparation of Figure 1.

MEDICAL PROGRESS

PIGMENTATION OF THE SKIN*

HAROLD JEGHERS, M.D.†

BOSTON

THE color of the skin of patients is often of distinct diagnostic value. This is true not only for skin disease but also for a wide variety of systemic disorders likely to be encountered in the everyday practice of medicine. Standard textbooks on dermatology offer ready reference for orientation on the primary dermatologic diseases accompanied or followed by pigmentary changes in the skin. By contrast, information relative to the color of the skin in systemic diseases is widely scattered throughout the literature and is often difficult to locate without an extended search. Considerable advance

has been made in this field. It is the purpose of this progress report to present a summary and a key to the literature most likely to be available to the average physician. Wherever possible, attention is also called to typical photographs and color plates contained in these articles. Material for this review has been collected over the last eight years as patients presenting almost all diseases to be discussed were encountered at teaching exercises in the Medical Out Patient Department and on the wards of the Evans Memorial and the Boston City Hospital. During this time information relative to this subject was obtained from the literature, by correspondence or conversation with a number of physicians interested in these diseases and by personal observation of patients.

*From the Evans Memorial, Massachusetts Memorial Hospitals; the Fifth and Sixth (Boston University) Medical Services, Boston City Hospital; and the Department of Medicine, Boston University School of Medicine.

†Associate professor of medicine, Boston University School of Medicine; physician-in-chief, Fifth Medical Service, Boston City Hospital, and assistant physician, Clinical Staff, Evans Memorial, Massachusetts Memorial Hospitals.

NORMAL COLOR OF THE SKIN

Many attempts have been made to measure quantitatively and record the color of the skin in disease. A easy method is visual comparison of skin color with a series of color plaques. Rowntree and Brown¹ devised a universal skin tintometer, composed of nine separate color scales resembling somewhat the allqvist hemoglobin scale, that allowed evaluation of the skin color of anemia, jaundice, erythrosis, cyanosis and brown pigmentation. These color scales could be analyzed by the Munsell method of color measurement. The methods of Flagg² and Lewis³ (colored plate) for measurement of the degrees of cyanosis and the spinning color top method, widely used in anthropologic study of skin color of racial groups,⁴ are other examples. These methods have, however, not been generally used in clinical practice. Almost all physicians evaluate patient's skin color from visual impression. Knowledge of the causation of normal skin coloration and the pathogenesis of abnormal coloration will place this visual evaluation on a much more rational basis. More attention might be paid to this subject in the courses of applied physiology and physical diagnosis.

A brief summary of the histology of skin will aid in understanding the following discussion of skin pigmentations.⁵ From without inward the epidermal layer of the skin (epidermis) is composed of the stratum corneum (keratinized cells), the stratum acidum (clear acidophilic layer poorly defined except over the palms and soles), the stratum granulosum (a thin layer) and the stratum mucosum (the principal portion of the epidermis), which is attached to the dermis (corium) within and covered by the stratum granulosum without. Its inner surface is indented with papillary processes of the dermis that contain terminal capillary loops. The stratum mucosum is composed of a larger outer prickly-cell layer and a smaller basal layer of two or three rows of cells. Regularly distributed through the basal-layer portion are some clear cells (melanoblasts) that under certain stimuli enlarge, become dendritic and form melanin. Part of the melanin granules are carried outward and can be demonstrated in the outer layers of the skin. The superficial dermis contains cells (chromatophores) that can phagocytize but do not form melanin and that may also phagocytize other pigment complexes — metallic pigments, lipoids and so forth.

The most exact knowledge in this field is based on the spectrophotometric analysis of skin color, an approach pioneered in 1926 by Sheard and his associates.⁶⁻⁸ Sheard's work allowed skin color to be quantitatively evaluated in terms of relative luminosity, which tells how much of a standard source of light, such as sunlight, the given color is capable of reflecting; dominant wave length or hue, the latter an attribute of color that permits it to be classified as reddish, yellowish and so forth and depends on

wave length alone; and purity or saturation, which determines the degree of hue, establishing how vivid or distinct it is. Furthermore, specific absorption changes in spectrophotometric reflection curves enabled actual pigments to be identified. The role of melanin and hemoglobin was especially studied. Much valuable clinical information was obtained from the analysis of skin in disease by this method.⁶⁻⁸ Williams⁹ and Taussig and Williams¹⁰ successfully used an abridged spectrophotometer, which measured the reflected light through three successive filters, in studying the skin color of persons with skin cancer.

Using the Hardy recording spectrophotometer, developed in 1935, Edwards and Duntley¹¹ were able to study the quantitative distribution of pigments in the normal skin in a manner not possible with earlier instruments and also to identify pigments not previously noted. Briefly, this apparatus

records the reflectance of the intact living skin, giving an analysis by wave lengths over the entire visible spectrum, from the violet end at 400 millimicrons to the red end at 700 millimicrons. In the curve thus obtained, each pigment is identified by its characteristic absorption band. The amount of the pigment is indicated by the degree of absorption of the wave length of the band. Lowering of the reflectance at the particular wave length is therefore proportional to the amount of the pigment present.¹²

Analysis of normal subjects demonstrated five cutaneous pigments: melanin, a derived material described as melanoid, carotene, reduced hemoglobin and oxyhemoglobin.¹¹ The color of these pigments was subject to some modification by optical effects produced by the successive skin layers. This fundamental paper is well worth reading in the original.

Carotene

Edwards and Duntley¹¹ were able to demonstrate that carotene is important in all skin color and is not limited to patients with clinical carotenemia. They recognized the presence of carotene from its characteristic absorption in the blue region of the skin spectrum at 482 millimicrons. Carotene adds a strong yellow component to normal skin color. The normal quantitative bodily distribution of carotene is given in Figure 1, which is reproduced from their paper. It is at once apparent that the classic distribution of the yellow color in a severe case of clinically recognizable carotenemia is essentially an exaggeration of the physiologic normal distribution. Female subjects showed much more carotene throughout the skin than did male subjects. They also showed marked evidence of carotene deposition in the breast, abdomen and buttocks, regions of minimal carotene storage in the male. Carotene was not noted in the scrotum of male subjects, apparently because of complete replacement in this region of the subcutaneous fat by the dartos fibers.

Carotene is normally present not only in dermal and subcutaneous fat but also in the stratum corneum, and in amounts proportional to the thick-

ness of this epidermal layer, hence the prominence of the yellow color of the palms and soles in clinical carotenemia. Sebaceous matter contains a small quantity of carotene. Edwards and Duntley believe that carotene dissolved in the intercellular fluid is transmitted through the stratum mucosum to the stratum corneum. It is stored in the corneum because this layer, by virtue of its lipin content, has an affinity for the pigment, whereas the mucosum,

and very blond Whites whose ability to respond to light stimulus is minimal. The brunet always shows some secondarymentation (tanning). Some people, especially those with reddish hair and thin skin, manifest in a spotty form (freckles). Melanin is responsible for color effects in the skin varying through brown to black. The rare dominant yellow melanin lesion in children has been commented on,¹³ but a yellow hue, as in some types of freckles, is characteristic of the skin of women is generally poorer in melanin than that of men. The female areas of stratum corneum, such as the nape of the neck, the axilla and the axillas, however, show a higher melanin ratio than do the equivalent areas in the male. Androgens have a role in developing melanin.¹² Hamblen found the average daily androgenic excretion in the urine of true blonds to be distinctly lower than that of marked brunets.

It is generally agreed that the color of the skin is a faulty racial test unless correlated with other physical features of the body. Brunsting noted that although the percentage of melanin in the skin of Negroes was less than that of the skin of Japanese and Chinese than from that of the skin of the Chinese, the same hue prevailed in all. Edwards and Duntley's¹¹ study confirmed the idea that the color of the skin owes their characteristic colors only to the amount of melanin in the skin.

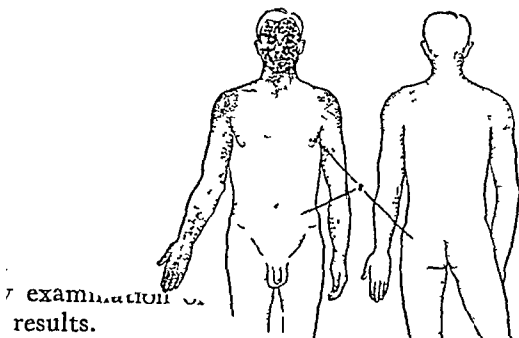


Fig. 1. Examination of results.

geographic study of the entire city should be undertaken, for it can safely be said that most patients in the sanatorium come from certain crowded districts in Charleston, South Carolina, and the North End. These areas are carefully checked. The number of patients admitted has been employed

Fig. 2. Distribution of Carotene (reprinted from Edwards and Duntley, with permission of the authors and publisher)

different chemical constitution, especially for carotene. A heavy stratum corneum overlying fat without contributing to its own. This, no doubt, is the characteristic lack of yellow in the skin of patients with marked carotenemia.

1. pigmentation is of two types. The pigmentation is controlled by racial factors and is responsible for the difference between a brunet and a blond. The skin of a Negro and also the regional pigmentation is emphasized in the normal increase in the color of the areolae, nipples and

Fig. 3. Distribution of melanin in the skin of different races.

PROGRESS

OF THE SKIN*

M.D.†

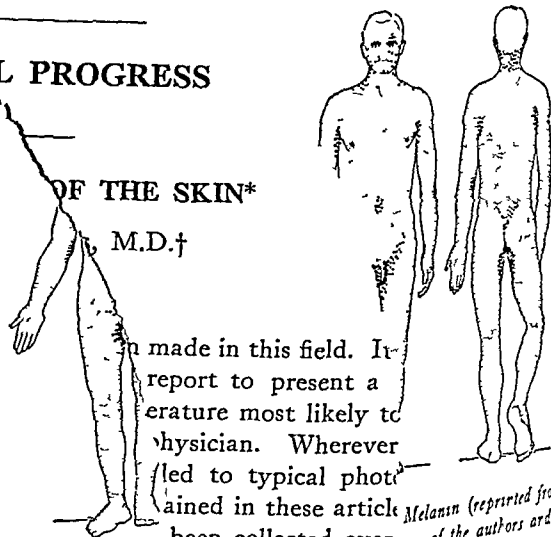


Fig. 2. Distribution of melanin in the skin of different races. (reprinted from Edwards and Duntley, with permission of the authors and publisher)

made in this field. It is our report to present a summary of the literature most likely to be of interest to the physician. Wherever possible, we have led to typical photographs of the skin obtained in these articles. Melanin (reprinted from Edwards and Duntley, with permission of the authors and publisher)

presenting almost all the melanin encountered at teaching hospitals. Patient Department of the Memorial and the National Cancer Institute, these findings are found in Whites and other than those obtained from the Negroes, and the general distribution is identical in the dark-skinned races. The distribution of melanin pigment in the skin of patients with diseases of the skin is of interest in these diseases. The pigment contained in the skin of patients with diseases of the skin is of interest in these diseases.

Melanin is formed by melanoblasts, specialized cells in the basal layer of the epidermis at the junction of the epidermis and dermis. It occurs as microscopic granules in palisade cells of the basal layer of the epidermis, in decreasing amounts toward the stratum corneum, with but little melanin in the chromatophores of the corium except in the eyelids and axillas of some persons. Melanin is absent in albinos, present in the smallest amount in blonds, more noticeable in brunets and present in the largest amounts in the darker racial groups.^{11, 15}

Melanin is an endogenous body pigment whose mechanism of formation is not clearly understood but is in some respects controversial.¹⁵⁻²⁵ There is evidence that the metabolism of the amino acid tyrosine is in some way related to its formation. The metabolism of the amino acid phenylalanine is probably also related to pigment metabolism. Under certain circumstances phenylalanine is converted to tyrosine. In vitro studies show that tyrosinase acting with tyrosine forms a melanin-like pigment. Active melanin-producing melanoblasts are believed by many to contain an enzyme (dopa-oxydase) that causes a dark cytoplasmic reaction when a fresh section of skin tissue containing them is placed in a solution of dihydroxyphenylalanine (abbreviated to "Dopa"). A positive Dopa reaction is an indicator of the existence of the faculty of natural melanin production, however, not of the presence of melanin itself. Other epidermal cells and the melanophores of the corium are not Dopa-positive even though they may contain melanin. Controversy still continues concerning the exact meaning of the reaction; nevertheless, the test has much proved merit.^{15, 17} Melanoblasts, after having formed melanin, transport the pigment granules to the epithelial cells, and some are phagocytosed by the dermal melanophores. The sites of excretion of melanin appear to be from the skin by desquamation, through the intestinal tract and through the kidneys.¹⁸ Under certain conditions, especially with metastases from melanotic tumors a gross amount may occur in the urine (melanuria). The ingestion of melanin in foods and synthesis in the intestines may account for much of the pigments in melanosis coli.¹⁸

The chemical similarity of the amino acid tyrosine to the hormone of the adrenal medulla, epinephrine, to the thyroid hormone, thyroxine, and di-iodotyrosine, and of the amino acid phenylalanine to Dopa is worth keeping in mind. Dopa and tyrosinase have not been demonstrated in the human body, but some such similar mechanism for melanin formation is suspected. Melanin metabolism is undoubtedly influenced by pituitary, adrenal and thyroid activity, by the activity of a number of vitamins (A, C and parts of the B complex) and probably by the nervous system, since some writers believe that parasympathetic predominance stimu-

lates pigmentation formation, whereas sympathetic predominance inhibits it.^{22, 25} Many external factors acting on the skin, such as sunlight, artificial ultraviolet rays, x-rays, thorium rays, heat, mechanical irritation and chemical irritation, cause varying degrees of melanin pigmentation. A variable number of these factors, and probably others as yet unknown, may in a complex manner initiate melanin production in disease. It is apparent that analysis of the cause of increased melanin pigmentation in any single case is by no means an easy matter.

Melanoid

Disintegration of melanin particles gives rise to a diffuse pigment in the epidermis, first noted spectrophotometrically in the skin by Edwards and Duntley¹¹ and named melanoid. Melanoid has, on spectrophotometric analysis, a characteristic absorption, with its maximum slope resembling melanin but shifted from the ultraviolet to the visible violet, thus allowing it to be identified in the spectral reflection curve. They are inclined to believe that it tends to make the skin a yellow of higher purity than does any yellow that can be produced by melanin. The amount in any region depends on the degree of its formation and storage, its formation being related to the concentration of melanin in that particular locality, and its storage to the thickness of the epidermis; the latter is especially true where the stratum corneum (stored dead epithelium) is thick, but holds only to a negligible degree where the stratum mucosum (proliferating epithelium) is heavy and the corneum is thin. Melanoid storage is high in the soles and probably the palms, and minimal in the areas of heavy stratum mucosum in the buttocks, back, cheeks and neck. Furthermore, the turbidity of a thick stratum mucosum causes the optical effect of scattering and raises the blue end of the spectrum, masking the presence of melanoid. For this reason Edwards and Duntley were unable to chart accurately its quantitative distribution.

Oxyhemoglobin

The hemoglobin of blood is present as a varying mixture of oxyhemoglobin and reduced hemoglobin, both of which have such characteristic absorption bands and transmission peaks that recognition of their presence in a spectral reflection curve from the skin is relatively easy. Hemoglobin varies from 90 to 95 per cent oxyhemoglobin in arterial blood to approximately 50 per cent reduced hemoglobin in venous blood. Relative amounts of arterial and venous blood in the skin can thus be determined. Edwards and Duntley¹¹ found the oxyhemoglobin spectral pattern to be especially prominent in the regions of skin where there is a rich arterial supply and where, for the most part, dermal papillae with their contained capillaries are high. These areas are the red parts of the head and neck, the nipples

ness of this epidermal layer; hence the prominence of the yellow color of the palms and soles in clinical carotenemia. Sebaceous matter contains a small quantity of carotene. Edwards and Duntley believe that carotene dissolved in the intercellular fluid is transmitted through the stratum mucosum to the stratum corneum. It is stored in the corneum because this layer, by virtue of its lipin content, has an affinity for the pigment, whereas the mucosum,

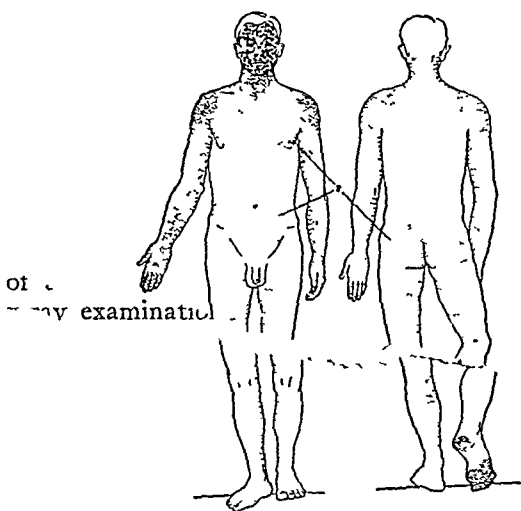


FIGURE 1. *Distribution of Carotene* (reprinted from Edwards and Duntley,¹¹ with permission of the authors and publisher).

by virtue of a different chemical constitution, possesses no affinity for carotene. A heavy stratum mucosum without much overlying corneum effectively screens the underlying fat without contributing any carotene of its own. This, no doubt, is the explanation for the characteristic lack of yellow in the eyes and mouth of patients with marked carotenemia.

Melanin

Normal melanin pigmentation is of two types. Primary or native pigmentation is controlled by constitutional and racial factors and is responsible for the difference between a brunet and a blond White, the darkness of a Negro and also the regional characteristics exemplified in the normal increase of melanization of skin of the eyelids, nipples and scrotum.¹¹ Secondary or acquired pigmentation varies with exposure to sunlight and disappears after removal of this stimulus. The pattern of primary pigmentation has been difficult to determine accurately because of the varying degree of secondary pigmentation that all persons acquire. Nevertheless, fairly accurate estimates have been made. Utilizing their own and other available data, Edwards and Duntley have plotted the normal bodily distribution of melanin (Fig. 2). They emphasize that this primary pattern is best exemplified in members of the dark races, in whom the primary melanin layer protects from average sun exposure,

and very blond Whites whose ability to resist light stimulus is minimal. The average brunet always shows some secondary melanization (tanning). Some people, especially with reddish hair and thin skin, manifest melanization in a spotty form (freckles). Melanin is responsible for color effects in the skin varying from through brown to black. The rarity of a dominant yellow melanin lesion in clinical practice has been commented on,¹³ but a yellowish hue, as in some types of freckles, is common. Skin of women is generally poorer in melanin than that of men. The female areas of strong primary melanin, such as the nape of the neck, the axilla and the axillas, however, show a comparatively higher melanin ratio than do the equivalent areas in the male. Androgens have an important role in developing melanin.¹² Hamblen and Calkins found the average daily androgenic titer in the urine of true blonds to be distinctly lower than that of marked brunets.

It is generally agreed that the color of the skin is a faulty racial test unless correlated with physical features of the body. Brunsting and Sorenson noted that although the percentage of melanin luminosity was less from the skin of Negro, Indian, Japanese and Chinese than from that of white persons, the same hue prevailed in all. Edwards and Duntley's¹¹ study confirmed the idea that the characteristic colors of races owe their characteristic colors only to

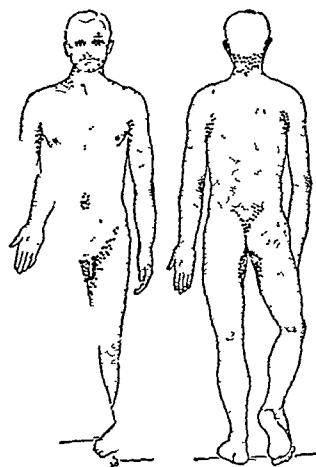


FIGURE 2. *Distribution of Melanin* (reprinted from Edwards and Duntley,¹¹ with permission of the authors and publisher).

tions in the amount of the melanin and, they add, melanin is the pigment melanoid. No other pigment is found in Whites and is countered in these found in the general population of the pigmented races, and the general pattern of the pigment is identical in the groups. Indians and Negroes have a "redskin" arose from the custom of painting faces and not to the custom of painting the skin.⁷

Physicians are familiar with the red color produced by transilluminating living tissue (Fig. 5). They are, however, much less familiar with the importance of the blue color produced by the scattering phenomenon (Fig. 5).

The five skin pigments have in common a preponderant absorption in the blue end of the spectrum, so that were it not for the scattering phenomenon of the normal stratum mucosum, which tends to raise the blue end of the reflected spectrum, the skin would be much redder than it is.¹¹ Comment has already been made that the blue hue induced by the scattering phenomenon is offset in certain areas by the absorption of the melanoid. Variations in skin thickness, especially of the stratum mucosum,

the color is slate gray, and in unusual instances where pigment is deep in the dermis, the color is blue.¹² Other pigments present below the epidermis — silver, iron, carbon and so forth — may cause this phenomenon. It is thus apparent that the same pigment can cause variations in skin color depending not only on the amount present but on the level of the skin at which it is present.

Melanoblasts producing melanin in the corium account for the blue color of the blue nevus²⁶ and of Mongolian spots^{27, 28} (see colored plate²⁵). Diffuse melanin pigmentation in the corium may cause the subject to appear diffusely blue,^{29, 30} (see colored plate²⁹). Pigment deposited in the corium accounts for the blue color of the *taches bleues* from the

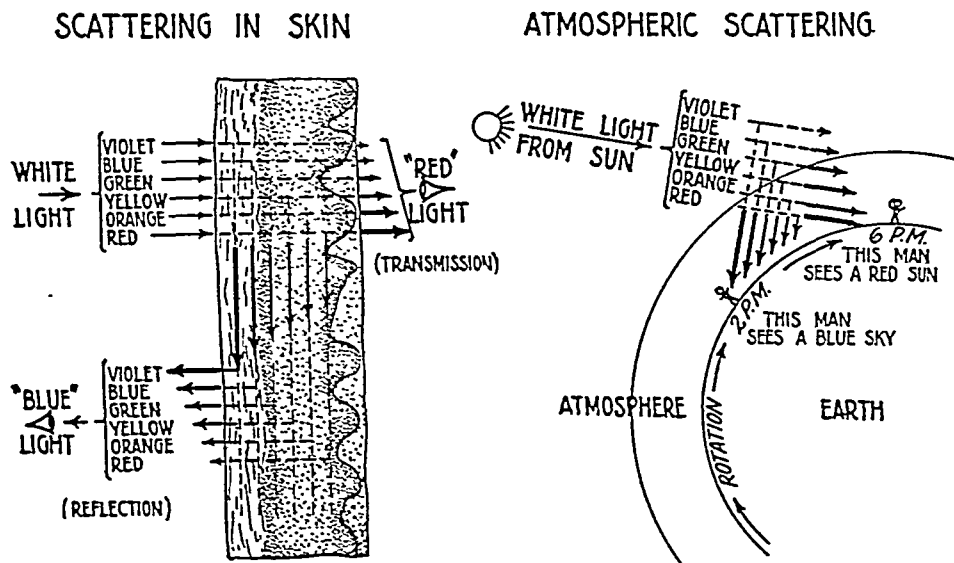


FIGURE 5. Diagrammatic Representation of the Process of Scattering (reprinted from Edwards and Duntley,¹¹ with permission of the authors and publisher).

cause this degree of scattering to vary likewise. The blue color of the larger superficial veins is dependent on this phenomenon. Hemoglobin is present in sufficient quantity to absorb all light striking it. Light cannot pass beyond the vessel into the subcutaneous tissue as it commonly does, so that the usual portion of the total skin reflection from the deeper tissues — predominant red (Fig. 5) — is thus absent. Skin reflection is entirely due to the predominantly blue light reflected from the turbid epidermis and turbid vein wall.

Melanin pigment in chromatophores in the corium if present in sufficient amount behaves in a similar manner, absorbing red rays and reflecting predominantly blue rays so that it appears as blue pigment beneath the skin. Other variations are possible. Becker and Obermayer¹⁵ summarize the color-producing properties of melanin in these words: "When a large amount of melanin is present in the epidermis, the color of the skin is brown, when predominantly in the dermal chromatophores (histiocytes) without too much epidermal pigment,

bites of *Pediculosis pubis*,³¹ the blue spots produced by hypodermic injections in drug addicts³²⁻³⁴ who use rusty needles or those with carbon particles from sterilizing in a flame (colored plate³⁴); the blue color produced by the black ink used by tattoo artists, the blue color of purpura when free blood is deep in the tissues,³⁵ probably the blue color of pinta in the pigmented phase and so forth.

Increased melanin in chromatophores probably explains some of the bluish color about the eyelids and in the axillas noted in certain persons. Bluish color caused by pigment in the hair shafts of the shaved male cheek is another physiologic example.¹¹ A shaved axilla no doubt may likewise show a bluish hue.

Anatomic Variations in Epidermis and Mucous Membranes

The normal epidermis varies in different areas of the body, not only in total thickness but in the relative thickness of each of its component layers. The influence of these normal anatomic variations on

the palms, the soles, the region of tuber ischii and the extensor surfaces of the joints. The quantitative bodily distribution of the predominant arterial blood pattern is given in Figure 3.

As is well known, oxyhemoglobin supplies a red component to skin color. Several factors that tend to suppress the oxyhemoglobin bands are present in the skin. The first of these is the increased reduced hemoglobin present in the venous limb of the capillary loop and in the subcapillary plexus with its strong venous blood component. Second, melanin, by its absorption across the spectrum, depresses the entire spectral reflection curve and thus tends to blunt the bands of oxyhemoglobin. This pigment, in proportion to its density, acts as a screen to prevent the superficial blood from attaining visibility. The difficulty of detecting erythema in a dark-skinned Negro is a representative clinical example of this phenomenon. Third, the turbidity of the stratum mucosum overlying the capillary loops adds the optical phenomenon of scattering and raises the blue end of the spectral curve. Brunsting and Sheard's⁸ study of the color of bloodless cadaver skin showed the major influence that blood in the superficial capillaries exerts on the color of the skin.

Reduced Hemoglobin

Parts of the body where the papillas are small or absent and where the subpapillary veins are more

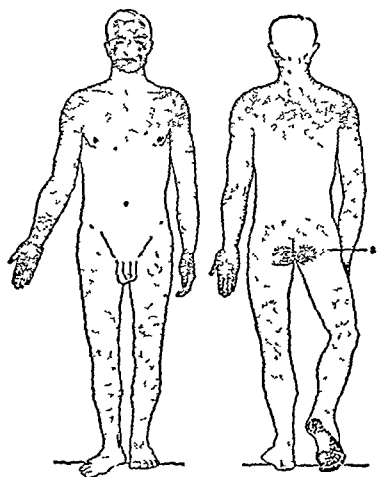


FIGURE 3. Distribution of Arterial Blood (reprinted from Edwards and Duntley,¹¹ with permission of the authors and publisher).

prominent have no special predominance of either form of hemoglobin. Edwards and Duntley¹¹ denote these areas by the absence of dots (Figs. 3 and 4). In certain areas they noted a real predominance of reduced hemoglobin, probably due to dilated veins and a sluggish flow, as well as the factors minimizing the oxyhemoglobin color that have already been commented on. This phenomenon was

marked in the dorsum of the feet, and in the lower parts of the trunk, including the belly, scrotum, loins and buttocks, the last especially in the male. These areas are rich in superficial and comparatively dilated veins, possibly owing to the effect of gravity

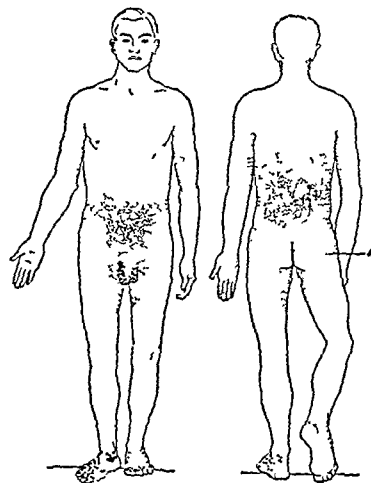


FIGURE 4. Distribution of Venous Blood (reprinted from Edwards and Duntley,¹¹ with permission of the authors and publisher).

Figure 4 contains a diagram of the bodily distribution of these areas.

Reduced hemoglobin adds a blue component to all skin color and becomes predominantly noticeable in true cyanosis.

ANATOMIC AND OPTICAL MODIFIERS OF SKIN COLOR

The color of the skin produced by its five normal pigments is subject to modification by anatomic differences in the various parts of the body surface and the optical effect of the scattering phenomenon. These factors are responsible in part for all skin color, and especially in pathologic conditions in which they may form the mechanism for bizarre and decided variations from normal skin color.

Scattering Phenomenon

The significance of the phenomenon of scattering as a modifier of skin color has been especially emphasized by Edwards and Duntley.¹¹ Scattering is defined as the rearrangement of light as it passes through a turbid medium; the quantity of light transmitted contains a greater proportion of long wave lengths (red), whereas the light that is scattered to the sides or back to the surface of the medium contains a correspondingly large proportion of short wave lengths (blue). For example, the atmospheric air is a diffuse turbid medium and is responsible for the blueness of the sky at midday and its redness at sunset (Fig. 5). The relatively transparent stratum corneum shows only slight scattering, whereas the turbid stratum mucosum exhibits the phenomenon to a marked degree. All

uated in essentially the same areas in which it is normally most marked (Fig. 1). Lack of yellow color of the scleras immediately distinguishes it from jaundice (see colored plates⁴¹). Routine inspection of the palms of patients for yellow color easily suggests this diagnosis. It should be confirmed by the three-layer test of Greene and Blackford.⁴⁰

Jaundice

The aspects of jaundice relative to its influence on skin color appear to be poorly understood. The small amount of bilirubin normally present in the blood and tissues appears to play no detectable role in the causation of normal skin color. It was not detected spectrophotometrically by Edwards and Duntley⁴¹ in their study of the normal skin. The icterus index of blood must therefore increase well over its normal level of 4 to 6, probably well beyond 15 to 25, before it becomes clinically detectable. For the last five years the Fifth and Sixth Medical Services of the Boston City Hospital have performed an icterus index test, using the Wintrobe⁴² macroscopic examination of blood, routinely on every patient admitted. Experience has shown that jaundice was readily overlooked on the routine admission clinical examination even when the icterus index ranged over 50. Failure to examine patients with good illumination, preferably daylight, was chiefly responsible. It was the impression that tissue staining (clinically detectable) lagged behind plasma staining (measured by the icterus index) in the early phase of jaundice, the reverse being true as the improvement set in.

The color of the skin in jaundice is variable and has been described as varying from faint yellow through deep yellow, orange, saffron, yellowish green, green and even bronze or dark brown. It is a commonly held clinical belief that the tint of jaundice may be of some diagnostic significance. Some of these tints, as listed in Lichtman's⁴³ monograph, are orange or saffron in intrahepatic jaundice, greenish to bronze in obstructive jaundice, green in intrahepatic jaundice in the presence of liver necrosis and also in the receding stages of jaundice and olive green in cholangitis and cholangitic cirrhosis. The orange color has theoretically been attributed to bilirubin or the bilirubin pro-pigment, xanthorubin, and the green hue to biliverdin, the oxidation product of bilirubin.⁴³ Watson's⁴⁴ quantitative study of bile pigments has served to place these clinical impressions on a rational basis. Using the Evelyn photoelectric colorimeter he quantitatively measured the amount of biliverdin present in the serum of various types of jaundice. It was not found in pure retention jaundice. Perhaps the absence of biliverdin accounts for the lemon yellow of the retention jaundice of pernicious anemia. In regurgitation jaundice, whatever the cause, some biliverdin was noted regularly. Only in jaundice due to cancer

did it exceed 1.0 mg. per 100 cc. Watson's observations were in accord with the clinical impression that outspoken biliverdin jaundice is most frequently due to cancer of the biliary tract. A few marked exceptions were noted in parenchymal jaundice due to subacute or prolonged hepatitis or cirrhosis.

Jaundiced persons who look bronze or brown may have in addition melanin pigmentation. Scratching from pruritus and avitaminosis, both commonly present with long-persistent jaundice, are among the commonest causes for development of melanin pigmentation of the skin.

Wearn⁴⁵ has re-emphasized the diagnostic value of a sign but rarely referred to in the modern medical literature. It is described as a yellowish-blue or perhaps greenish color of the skin produced by a combination of the yellow of jaundice and the bluish purple of cyanosis. It is considered almost pathognomonic of an organic tricuspid lesion or a relative insufficiency of the valve. Wearn noted it in 17 of 24 cases. At times, jaundice and cyanosis occur together in other conditions, but their occurrence in other forms of heart disease is not frequent, and differentiation is not difficult.

Jaundice of prolonged duration during infancy may permanently stain with a green color the deciduous teeth forming during this time^{46, 47} (see colored plate⁴⁶).

Elastic tissue has a great affinity for bilirubin and is called "bilirubinophilic." This accounts for the ready pigmentation of the skin, sclera, blood vessels and cornea, which are rich in these fibers,⁴⁸ and its persistence after other body tissues have cleared. Distribution of these fibers probably accounts for the greater degree of pigmentation noted in the upper parts of the body.¹³

Meakins^{37, 38} and others³⁹ have commented on the absence of jaundice in edematous areas (see colored plate³⁷). This curious phenomenon explains the mechanism of the unilateral jaundice syndrome reported by Page,³⁹ who described it in 2 patients with cardiac failure and hemiplegia. Edema appeared only on the paralyzed side, whereas jaundice appeared on the other side. Jaundice in persons with one glass eye presents, on first glance only, the impression of looking at a person with unilateral jaundice.

A wheal formed by injecting histamine into jaundiced skin increases capillary permeability for bilirubin so that the wheal is yellower than the surrounding skin. The yellowish line bordered by two red lines formed by streaking the skin lightly (icterographia) is a similar phenomenon.⁴³ These procedures can be used as a simple skin test for latent or mild jaundice.⁴⁵⁻⁵⁰

Atabrine Pigmentation

The ability of the widely used antimalaria drug atabrine to produce frequently a yellowish pig-

skin color has already been commented on. For anatomical reasons, the color of mucous membrane is quite different from that of the body skin. Any anatomic change in the epidermis or mucous membrane may therefore act to modify its color. In general, thinner epidermis is more transparent and allows the blood in the dermal papillas and superficial dermis to shine through. Thicker epidermis is less transparent and looks yellower.³⁶

Variations in Capillary Blood Flow

Capillary blood flow through the skin is not constant but subject to many physiologic variations, causing the color produced by the contained blood pigments to vary accordingly. Brunsting and

The influence of edema on the distribution of pigment in the skin has been especially commented on.³⁷⁻³⁹

* * *

The term "pigmentation of the skin" as used in this review implies a change from normal of color of the skin, whether due to pigments present in the tissues or to those in the blood passing through the skin. The basic work of Sheard⁸ and Edwards and Duntley¹¹ shows clearly that color depends on both these factors. It appears to be much more rational and in keeping with physiologic principles always to think of skin color in this manner. Table 1 gives in tabular form a classification of abnormal skin color (pigmentation).

TABLE 1. *Classification of Skin Pigmentations* of General Medical Interest.*

ANATOMIC AND OPTICAL MODIFIERS OF SKIN COLOR	
Scattering phenomenon	
Anatomic variations in epidermis and mucous membranes	
Variations in capillary blood flow	
Edema of skin	
YELLOW PIGMENTATIONS	
Pigmentation of myxedema	
Pigmentation of uremia	
Dinitrophenol pigmentation	
Industrial staining	
Picric acid pigmentation	
Carotenemia and carotenoderma	
Jaundice	
Atabrine pigmentation	
Local discoloration of abdominal wall:	
Cullen's sign	
Grey-Turner's sign	
Xanthomatosis	
Miscellaneous	
MELANIN PIGMENTATIONS (see Table 2)	
HEMOGLOBIN PIGMENTATIONS	
Diminished amount of hemoglobin	
Increased amount of hemoglobin	
Predominance of oxyhemoglobin	
Predominance of reduced hemoglobin	
Methemoglobinemia	
Sulfhemoglobinemia	
Carboxyhemoglobinemia	
Cyanhemoglobinemia	
Nitric oxide hemoglobinemia	
METALLIC PIGMENTATIONS	
Hemochromatosis	
Hemosiderosis	
Argyria	
Chrysiasis	
Bismuthia	
Hydrargyria	
Lead pigmentation	
Iron pigmentation	
MISCELLANEOUS PIGMENTATIONS	
Porphyria	
Methemalbuminemia	
Malarial pigmentation	
Pigmentation due to other medicinal agents	
Unclassified pigmentations	

*As implied here, skin pigmentations may be localized or generalized, and are not primarily related or due to changes in the texture of the skin or to local skin lesions. The term "skin pigmentation" is used to designate changes in skin color due both to deposition of pigments in the skin and to pigments present in the blood.

Sheard⁸ give representative examples, such as vasodilatation following change to a warm environment, drinking of alcoholic beverages, local irritation from friction and an emotional disturbance with blushing, all making the skin redder, and vasoconstriction from environmental exposure to cold or the blanching caused by fear, giving a paler appearance. Pathologic processes can also cause profound change in skin color by varying the capillary blood flow.

Edema of Skin

Macerated skin is whiter than normal skin.¹⁵ Likewise, the presence of edema of the skin has a profound influence on skin color, as witness the pallor out of all proportion to the degree of anemia noted in patients with generalized edema of the nephrotic syndrome. Another example is the partial loss of pigmentation noted in some persons with Addison's disease due to the edema caused by desoxycorticosterone therapy and the rapid reappearance of pigmentation when they become dehydrated with the onset of an Addisonian crisis.

that is based on the above physiologic principles. This review primarily considers disorders of general medical interest and for the most part does not include dermatologic disorders. Throughout, attempts have been made wherever possible to crystallize working ideas and clinically useful axioms.

YELLOW PIGMENTATIONS OF THE SKIN

Carotenemia and Carotenoderma

The work of Edwards and Duntley¹¹ clearly shows that the pigment carotene contributes a yellow component to the color of the skin of all normal persons. This being so, carotenemia and carotenoderma of clinical significance are merely exaggerations of the normal minimal yellow color of serum and skin, respectively. This subject was viewed in detail last year in a progress report in this journal.⁴⁰ The yellow of carotenoderma is canary or lemon in hue, in contrast to the brown orange, saffron or green tint of jaundice (see color plates⁴¹). When clinically significant it is accom-

latous patients. Escamilla found carotenemia in consecutive cases of untreated myxedema, and similar findings were noted in 2 cases recently studied at the Boston City Hospital. Carotenemia has also been noted in Simmonds's disease⁵⁸ and in castrate and eunuchoid men.¹²

Krantz and Means⁶³ report 6 cases of myxedema manifesting areas of brownish pigmentation of the skin, more pronounced on exposed surfaces of the body. This pigmentation had appeared coincidentally with, or shortly after, the onset of symptoms of myxedema and cleared up promptly under thyroid administration. There was no pigmentation of the mouth. The description given in this paper is suggestive of chloasma areas of melanin pigmentation. The scarcity of such reports in the literature and the lack of similar descriptions in the current textbooks and monographs strongly suggest that a noticeable degree of generalized or localized melanin pigmentation of the skin in myxedema is not a frequent finding. It may possibly be explained as some fortuitous circumstance in the given case.

Pigmentation of Uremia

The skin in patients with long-standing renal failure is often of a peculiar pale, yellowish, yellowish-brown or buckwheat tint. Anemia undoubtedly accounts for the pallor. Becher⁶⁴ believes that, in renal insufficiency, chromogens of urine pigments are retained in the blood and become stored in the tissues and skin. The yellowish discoloration is most pronounced on the face and hands because under the influence of light the chromogens are changed into pigments as the result of oxidative processes. The light color of the urine in patients with uremia is believed to be due partly to retention of chromogens in the blood and in tissues and partly to an inability of the kidneys to oxidize these pro-pigments to pigments.⁶⁵

Boeck and Yater⁶⁶ noted carotenoderma in 10 per cent and carotenemia in 100 per cent of a group of kidney cases. It seems likely that carotenemia contributes to the pigmentation of patients with uremia. This has been attributed to poor urinary excretion of the carotenoid pigments, but the extent of urinary loss of carotene normally sustained is by no means agreed on.⁶⁶⁻⁶⁸

The brownish tint of the skin noted occasionally in patients with uremia is impressive. Whether any increase in skin melanin occurs is not known. Generalized pruritus is a common symptom in uremia. The resultant scratching irritates and mildly traumatizes the skin. Malnutrition is likewise frequent in uremic patients. These are among the known stimulants for an increase in melanin pigmentation of the skin, which may be additive to and blended with the underlying yellowish pigmentation of uremia. An excess of a hormone of the pars intermedia affecting pigmentation is men-

tioned as present in uremia.⁶⁹ What part, if any, this plays in the pigmentary syndrome of uremia of human beings is not known.

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American physicians became familiar with 2-4-dinitrophenol in 1933, when because of its metabolic stimulating properties it was used for the treatment of obesity.⁷¹ For a time it was widely used for weight reduction, both by prescription and in numerous proprietary preparations. The many reports of toxic reactions from its use led to its general withdrawal as a therapeutic agent. Of interest here was the observation that dinitrophenol often discolors the scleras and even the skin, thus simulating the clinical appearance of jaundice.⁷² The discoloration is due to the drug in the plasma and body tissues. It varies from time to time and disappears gradually after ingestion of the drug is discontinued. Since it colors serum and plasma, it may give false high values for the blood icterus index. This can be avoided by determining the index on blood plasma that has been acidified.⁷²

Except in rare cases, dinitrophenol does not cause liver damage and jaundice.^{72, 73} Liver function is usually normal.^{74, 75} The yellow color is purely one of staining tissue and blood. If yellow pigmentation due to dinitrophenol is suspected, the diagnosis can be established on the basis of a history of using a remedy for weight reduction and determination of the icterus index with acidified plasma as compared to nonacidified plasma.

Staining Due to Substances of Industrial Origin

There are a number of chemicals used in certain industries that produce yellow staining of the skin in employees exposed to or handling them. An important one of these is tetryl, or trinitrophenyl-methylnitramine, a pale-yellow crystalline powder that is an important ingredient in explosives. Employees handling tetryl powder frequently develop a yellow staining of the hands in one to three days and of the face, neck, scalp and hair in one to three weeks.⁷⁶ This color deepens on exposure to sunlight and becomes more prominent during the summer.⁷⁵ In industry the terms "canary" and "tetryl blond" are frequently used to describe persons with

mentation of the skin is by now known to many physicians. The review by Schechter and Taylor⁵¹ dealing with atabrine pigmentation has served to emphasize the importance of this subject. This pigmentation may closely simulate jaundice and lead to diagnostic error. This is especially true if it persists for months and a different physician than the one who ordered the drug sees the patient some time after this medication was discontinued.

The skin pigmentation is noticeable within three to ten days of beginning oral therapy and may persist for a few weeks to as long as four months after discontinuance of the drug.^{51, 52} Parenteral administration of the soluble form of the drug does not eliminate the possibility of pigmentation.⁵¹

The pigmentation is diffuse and most prominent on the dorsum of the hands, arms and feet. It appears on the forehead and face and may form a golden ring around the mouth.⁵¹ Soni⁵² has emphasized that the pigmentation is usually most marked on the exposed parts of the body. It may also be accentuated in the interdigital skin folds and neck creases and under the breasts.⁵¹ No changes occur in the texture of the skin.⁵² The color has been variously described as lemon, greenish yellow, golden yellow and turmeric, but in any event a yellow component is clearly evident. A medical officer has described it as "a sickly greenish yellow."

Staining of the mucous membranes has not been emphasized in the printed reports and appears to be less reliable and noticeable than the skin color. Schechter and Taylor⁵¹ emphasize that contrary to the experience of others they have failed to notice any significant discoloration of the scleras, a point that is in accord with the extensive experience of two Army medical officers who discussed this subject with me. Further observations will no doubt settle this question. Martin, Cominole and Clark⁵³ noted yellowish discoloration of the scleras in experimental animals receiving toxic doses of atabrine (0.1 to 0.2 gm. per kilogram of body weight), but not when the dosage was reduced to 0.05 gm. Perhaps the same phenomenon occurs in human beings. If found consistently, the lack of significant scleral pigmentation would readily differentiate atabrine pigmentation and jaundice. Atabrine pigmentation can be distinguished from carotenemia by the deeper pigmentation of the dorsum of the hands in the former and of the palms and soles in the latter.⁵¹ Yellow staining of the skin from chemicals must naturally be eliminated. Quinine does not cause pigmentation.⁵² Plasmochin in toxic doses may cause cyanosis from methemoglobinemia.

Atabrine pigmentation appears to result from deposition of the dye in the skin rather than from a secondary metabolic disturbance or liver damage.⁵¹⁻⁵³ Hecht⁵⁴ demonstrated that the pigment found in animals was fluorescent, which suggested

that it was either atabrine or a breakdown product thereof. Atabrine does not cause liver damage except possibly when diminished glycogen reserve from malnutrition is present.⁵⁴ Ruge⁵⁵ has presented data indicating that chemical and clinical reactions characteristic of hepatic damage in acute malaria return to normal under atabrine therapy. Atabrine pigmentation, if prolonged, may be indicative of accumulation of the drug. Constipation, anemia and exhaustion from infectious disease are believed to augment the intensity and duration of the pigmentation.^{51, 52} The more marked accentuation of the pigmentation on the exposed parts of the body has suggested some influence of the rays of the sun.⁵²

Tests for hyperbilirubinemia are necessary in suspected concurrent jaundice and atabrine pigmentation. Schechter and Taylor⁵¹ have outlined a simple laboratory procedure that detects atabrine even if only 0.02 mg. is present in the urine. Hansen⁵⁶ has reported on the use of atabrine take for the purpose of simulating jaundice.

Pigmentation of Myxedema

Descriptive terms such as sallow yellow, yellowish pallor, old-ivory tint, waxy yellow and slight icteric have been commonly used to describe the color of the skin in myxedema.^{57, 58} A malar flush or "a light spot of pink high in the center of the cheeks,"⁵⁷ yellowish sallowness of the rest of the face and the presence of edematous, coarse-looking features constitute the characteristic facies of myxedema (see colored plate⁵⁹). The pallor component of the color is readily explained by the high incidence of anemia in this disorder.⁵⁸ The myxedematous condition of the skin probably also contributes to the pallor.

The yellow component of the skin color is of special interest. Rarely pernicious anemia coexists with myxedema.⁶⁰ Under this and perhaps other exceptional circumstances bilirubin pigment may produce a yellow skin pigmentation in myxedema. In the vast majority of cases, however, this is not the cause. The recent reports by Escamilla and Mandelbaum et al.⁶¹ confirm earlier observations⁶² that the yellowish color so frequently noted in myxedema is due to carotenemia, which may occur in this disease even when the amount of carotene in the diet is low. According to Escamilla, the conversion of carotene to vitamin A in the liver is hindered by the depressing effect of the lowered metabolism and tends to improve gradually under treatment with thyroid substance. It is believed by some that the thyroid hormone is antagonistic to vitamin A and governs the rate of its consumption. In hypothyroidism the vitamin A in the serum is normal or low, whereas the carotene is increased. Careful inspection of the palms for a yellow color and Greene and Blackford's three-layer test of the serum should be done routinely in all myxedema.

jaundiced patients. Escamilla found carotenemia in consecutive cases of untreated myxedema, and similar findings were noted in 2 cases recently studied at the Boston City Hospital. Carotenemia has also been noted in Simmonds's disease⁵⁸ and in castrate and eunuchoid men.¹²

Krantz and Means⁶³ report 6 cases of myxedema manifesting areas of brownish pigmentation of the skin, more pronounced on exposed surfaces of the body. This pigmentation had appeared coincidentally with, or shortly after, the onset of symptoms of myxedema and cleared up promptly under thyroid administration. There was no pigmentation about the mouth. The description given in this paper is suggestive of chloasma areas of melanin pigmentation. The scarcity of such reports in the literature and the lack of similar descriptions in the current textbooks and monographs strongly suggest that a noticeable degree of generalized or localized melanin pigmentation of the skin in myxedema is not a frequent finding. It may possibly be explained as some fortuitous circumstance in the given case.

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this yellow staining of the hair, scalp and face.⁷⁶ It is not necessarily indicative of impending dermatitis. Tetryl dermatitis generally occurs between the second and the third week of exposure and is characterized by a burning, itching, erythematous, edematous rash of the circumoral region of the face and the lateral surfaces of the neck, and less frequently of the arms. It is often stated that tetryl produces only these local manifestations. Witkowski et al.⁷⁶ stress that systemic symptoms, such as epistaxis, sneezing, nonproductive cough, chest pain, anemia, increased irritability and anorexia, may occur. The presence of yellow staining aids in evaluating patients with industrial exposure. The history of occupational exposure, staining of the hair, the lack of yellow scleras and the fact that tetryl does not cause jaundice enable the physician to recognize readily the significance of the yellow staining.

Other substances handled industrially likewise stain exposed skin surfaces yellow in a manner similar to tetryl. Picric acid,⁷⁷ trinitrotoluene (see colored plate⁷⁸), styphnate, nitric acid⁷⁷ and the German explosive, hexanitrodiphenylamine,⁷⁷ are among the more important ones. In sharp contrast to tetryl, some of these may cause liver damage and true jaundice. Jaundice occurring in an industrial "canary" can readily be overlooked.

PICRIC ACID PIGMENTATION

Simulated Jaundice

Judging from the literature appearing during World War I, simulated jaundice as a form of malingering was evidently not uncommon in some of the European armies.⁷⁹⁻⁸¹ As a medical curiosity it ranks with the use of egg albumin in the urine to simulate albuminuria and injections of turpentine and paraffin to produce artificial abscesses.⁸² Simulated jaundice was produced by the oral ingestion of 5 to 10 cgm. of picric acid three times a day in pill form.⁷⁹⁻⁸² Within one or two days the skin and scleras became pigmented yellow and on routine clinical inspection the patient could pass as having jaundice. Vomiting, abdominal pain, anorexia, nausea and diarrhea were often noted. The urine was more likely to be orange to red than to have the usual bile-stained appearance, but was sometimes normal in color. A yellow color is due to staining of the tissues by picric acid, or more likely to a breakdown product such as picramic acid. The stain sometimes persisted for several weeks. A similar syndrome has been reported from picric acid absorbed from ointment used to treat an open wound.⁷⁹ Numerous tests of the urine and blood were devised to detect the simulation of jaundice from ingestion of picric acid.^{79, 80, 82, 83} The practice entailed danger, since picric acid is toxic to the liver and true jaundice from liver damage could be grafted onto the picture of pseudojaundice.^{81, 84}

From the scarcity of reports in the current literature it appears that simulated jaundice has been encountered during World War II or possibly has not been reported. Hansen⁸⁵ reports a ca simulation of jaundice by the use of atabrine.

Local Discoloration of Abdominal Wall

Cullen,⁸⁵ in 1919, described the occurrence of discoloration resembling a bruise at the umbilical area of a woman with a ruptured ectopic pregnancy and utilized this sign to make the correct operative diagnosis. The diagnostic value of this sign was confirmed by Hellendall,⁸⁶ Novak⁸⁷ and many others.⁸⁸ Smith and Wright⁸⁸ reviewed the literature in detail in 1935 and concluded that this sign is a rare indication of intraperitoneal hemorrhage. In the foreign literature it is sometimes known as the Hofstätter-Cullen-Hellendall sign. Most frequently it is called Cullen's sign and is considered diagnostic of intraperitoneal hemorrhage.

Two phenomena appear to have been described under this sign.⁸⁹ One is the bluish discoloration noted when intraperitoneal blood is seen through the thin tissue of an umbilicus, a hernia, an incision and so forth. The production of the bluish color apparently involves the same optical phenomenon as described previously for the blue color of skin veins. The other condition is the discoloration of the subcutaneous tissues about the umbilicus, incisions, near the anterosuperior spine of the ilium and in the loins. The color resembles a bruise; it is bluish at first, then becoming bluish green and finally yellowish (see colored plates^{85, 87, 90}). The term "Cullen's sign" should be applied to the latter phenomenon.⁸⁸ The changing shades of color have been explained as due to oxidation of blood elements traveling in the lymphatics connecting the umbilicus or incisional area with the peritoneal cavity.

Grey-Turner⁹¹ recorded similar local areas of pigmentation in 2 patients with hemorrhagic pancreatitis, in one case about the umbilicus and the other in the loins. Direct action of hemorrhagic pancreatic juice escaping by way of retroperitoneal tissue may have produced the loin pigmentation (see illustration⁹¹). The term "Grey-Turner's sign" has been applied to this phenomenon especially by English writers. Its value for diagnosis of acute hemorrhagic pancreatitis has been amply confirmed.^{89, 92, 93} Fallis⁸⁹ reports that in one clinical case the correct preoperative diagnosis was made in 3 of 35 cases on the basis of the clinical phenomenon of localized discoloration of the abdominal wall. This sign in acute pancreatitis should not be confused with the cyanosis described by Halsted⁹⁴ and others,^{95, 96} which may take on a mottled pattern and be distributed irregularly over the surface of the abdomen and even the extremities. It is probably a manifestation of peripheral circulatory collapse.

Yellowish pigmentation about the umbilicus due to rupture of the common bile duct was described by Ransohoff.⁹⁶ Other causes of hemoperitoneum besides ruptured ectopic pregnancy may cause this phenomenon. There is some evidence that extra-peritoneal spread of blood is responsible for this sign. It has been reported as present without free intraperitoneal blood and often absent with gross hemoperitoneum.^{88, 89} This sign can be readily overlooked unless searched for carefully with good illumination.

Miscellaneous Pigmentations

Skin lesions characterized by both a yellow color and a recognizable local gross change in skin morphology should not be confused with the type of yellow pigmentation discussed in this review. A clear orientation in this field is given by Weidman¹³ in his review of the many nonxanthomatous skin conditions characterized by a yellow hue, and by Montgomery⁹⁷ and Thannhauser and Magendantz⁹⁸ in accounting for the many different types of xanthomatous skin lesions. In xanthomatosis, the entire surface of the skin is sometimes tinted a chamois or pale yellow.⁹⁹ The whole skin area in so-called "systematized amyloidosis" may be of a waxy coloration.¹⁰⁰ Hansen⁵⁶ has commented on the yellow skin color that may result from the use of santonin or acriflavin. The earlier literature has emphasized the yellowish discoloration of the palms noted in persons with typhoid fever and known as "Filipovitch's sign."⁹⁹

A peculiar type of jaundice has been described as being present in the septicemias due to gas-bacillus infections, especially in the post-abortive group. The skin color varies from brownish yellow to mahogany. This color has been attributed to the presence in the plasma of bilirubin, oxyhemoglobin, hematin and methemoglobin.¹⁰¹

(To be continued)

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TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30291

PRESENTATION OF CASE

A forty-two-year-old teacher entered the hospital for study.

The patient had been in excellent health until four and a half months prior to entry, when he had an attack of chills, fever, cough, chest pain and rusty sputum. He spent five weeks in a hospital in another city, where he was given various sulfonamide derivatives without much benefit but finally recovered. Following discharge from the hospital he slowly gained 10 pounds. He had an occasional dry cough,

*On leave of absence.

but was getting along well until three weeks before admission, when a follow-up x-ray film of the chest taken by his physician showed a persistent lesion in the right upper lobe. He was then bronchoscoped in another city; a biopsy was said to have shown epidermoid carcinoma by one pathologist and squamous-cell metaplasia by another. There was no history of exposure to tuberculosis.

Physical examination showed a well-developed, well-nourished man in no distress. Examination was negative except for slight dullness over the right upper lobe, with increased tubular breathing below.

The blood pressure was 140 systolic, 85 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,680,000, with 14 gm. of hemoglobin. The white cell count was 9200. A blood Hinton test was negative. The urine was normal. The nonprotein nitrogen was 32.5 mg. per 100 cc.

X-ray examination of the chest (Fig. 1) showed partial collapse of the posterior medial segment of the right upper lobe. Within the area of collapse were several air-bearing areas, such as those seen in consolidation of the lung with an open bronchus. The right lower and middle lobes showed some

compensatory overexpansion. The right leaf of the diaphragm moved somewhat limitedly with respiration. The mediastinum was retracted to the right of the area of collapse. There were no evident hilar lymph nodes, pleural effusion or bone metastases. When compared with the films made elsewhere there

response of the fever or merely persistence of physical signs for four and a half months.

DR. BENJAMIN CASTLEMAN: They found a Type 2 pneumococcus in the sputum.

DR. BECKMAN: That is helpful because, of course, the presence of a Type 2 pneumococcus in the



FIGURE 1. *Roentgenogram of Chest*

seemed to have been some reventilation of the lung since the previous examination.

On the fourth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM BECKMAN: I find this case singularly lacking in details that I should like to have in order to make a definite diagnosis. It seems that there can be no doubt, with the initial symptoms four and a half months before admission of chills, fever, cough, chest pain and rusty sputum, that the patient had pneumonia of some sort. These are the characteristic features of pneumonia, and I do not believe anything else could produce that picture, although sometimes a pulmonary infarct may simulate it. I do not suppose that the details of the illness in the other hospital are available, but it would be interesting to know in just what way he did not respond to treatment—whether it was a lack of

sputum is uncommon unless it is producing disease. I suspect that it can occasionally inhabit the normal nasopharynx, but in general it indicates infection, which lends further proof to the idea that the patient had lobar pneumonia at the time of admission to the other hospital. Most likely he had a sulfonamide-fast organism or he would have responded better than he did, although we do not know the nature of the course in that hospital. Later, however, he gained 10 pounds to replace some of the weight that he had lost during that illness. Apparently he was in good health, except that the doctor thought he should have a check-up, following which he was advised to come here for study.

It seems to me that one can reason about this case in two ways. The first is that the lesion found at the time of the admission to this hospital was a sequela of the acute infection that he had had four and a half months before. The common complications of pneumonia are, of course, empyema and

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but was getting along well until three weeks before admission, when a follow-up x-ray film of the chest taken by his physician showed a persistent lesion in the right upper lobe. He was then bronchoscoped in another city; a biopsy was said to have shown epidermoid carcinoma by one pathologist and squamous-cell metaplasia by another. There was no history of exposure to tuberculosis.

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*On leave of absence.

ight resemble this. I was particularly interested what he had to say about the cases of lobar pneumonia that clear up not by resolution but by organization.

There are a number of features that are consistent with this under the heading of subacute and chronic durative pneumonia. He says, for example, that, when resolution does not take place, but instead there is organization of the exudate, one gets a type of induration that tends to contract, as this had done. He says that it is commoner in cases of pneumonia that have not responded as they should and where the fever has persisted, which is the case here. I was rather intrigued with these areas that might have been cavities, since Dr. Lord speaks of dilatation of the bronchi or cavities in the lung, which may give the breathing an amphoric quality. I therefore mention organizing pneumonia as a possibility in this case. I think that the case hinges on which pathologist was right. One said that he had cancer, and the other that he did not. If he had cancer, he had cancer!

DR. SWEET: I am pleased that this case was discussed here. I had hoped that Dr. Castleman would also present another case, which is a running mate of this one, the patient having been observed continuously at this hospital for a period of five months. The diagnosis was the same in both cases, and in both cases were mystifying before operation. Of course one must remember that the patient whose case is discussed here today was sent to me with a diagnosis of carcinoma of the bronchus of the right upper lobe. He and his family had been so informed. He was an apprehensive person and very much worried. It is obvious to those of you who are familiar with carcinoma of the lung that the opportunities to remove small, and perhaps curable, lesions are few and far between. Because I know the man who did the bronchoscopy, I was confident that I could rely entirely on the accuracy of his observation and that we could not have done any better here. So I did not have another bronchoscopy performed. I did get the slides and went over them with Dr. Ronald C. Sniffen, who did not agree with the diagnosis of carcinoma. I therefore made a diagnosis of collapse of the right upper lobe due to obstruction of a process beyond where one could see it with the bronchoscope.

The most frequent cause of that picture, in my experience, is tuberculosis. In other words the usual cause of occlusion of bronchi in the upper lobe is tuberculosis. But I did not believe that this man had tuberculosis. I cannot tell you exactly why. One reason was that he did not have acid-fast organisms in the sputum, and as Dr. Holmes has said, the x-ray picture did not look like that of tuberculosis. I ended up by operating in the hope that I might be getting ahead of an early carcinoma that could not be seen through the bronchoscope. When I got in, there was complete collapse of the

right upper lobe, as the x-ray shows. The lobe was densely adherent and exceedingly difficult to get out. In that respect it was very much like the lungs found in many cases of tuberculosis. On the other hand there was difficulty of dissection around the hilus of the lung, which is unlike tuberculosis. I left the operating room still with the impression of tuberculosis, but I did not know whether it was.

CLINICAL DIAGNOSIS

Carcinoma of lung?

DR. BECKMAN'S DIAGNOSIS

Bronchial tuberculosis.

ANATOMICAL DIAGNOSES

Chronic pneumonitis.

Bronchiectasis, slight.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The lobectomy specimen showed a fibrous, rubbery lesion, measuring 10 by 5 by 5 cm., in the anterior portion of the lobe, with a number of dilated bronchi close by. There was no obstruction to the bronchus of this lobe. Microscopic examination of the scarred area showed chronic pneumonitis, with exactly the picture that Dr. Lord described and to which Dr. Means referred. It apparently was an organized pneumonia with a great deal of fibrosis in which there were tiny cavities filled with air, apparently distended respiratory ducts and atria, and a slight degree of secondary bronchiectasis. The whole process, I am certain, was due to the unresolved pneumonia. There was no evidence of tumor or tuberculosis.

DR. SWEET: I would like to emphasize the point which was touched upon before; namely, if one waits in every case for a positive bronchoscopic biopsy in cases of carcinoma of the lung, the opportunity for successful surgical removal is frequently lost. If we are to improve our results in this dread disease, it will be necessary to explore many cases such as this in order to catch a few early cases of carcinoma before it is too late.

This patient left the hospital feeling well; he was much happier than when he came.

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CASE 30292

PRESENTATION OF CASE

A seventy-year-old Anglican priest entered the hospital because of severe substernal pain.

The patient had been in apparent good health until about two or four months before admission,

lung abscess, which do not seem probable, because he was in excellent health and had no evidence of constitutional disease — no fever and no loss of weight. If he had had a lung abscess and was not producing a large amount of sputum, one would expect fever and general constitutional symptoms. The other possibility along that line is that he developed pulmonary fibrosis, which seems to occur more frequently than we used to think, especially following a primary, atypical pneumonia. The other line of reasoning that one might pursue is that the patient had had some lesion in the lung prior to the illness and that the physical signs were present at that time and persisted through the acute illness without bearing a distinct relation to it. He might have had a benign bronchial adenoma that produced collapse of the lung and acute infection behind the obstruction or he might have had a malignant bronchial tumor. I do not believe that that is likely. There was a rather striking difference of opinion among the pathologists with respect to the biopsy. The clinical picture did not resemble that usually encountered in carcinoma of the lung. He had had no persistent cough and no hemoptysis. Also, if he had had cancer, I should not have expected his symptoms to regress in the way they did; it is more usual for a primary cancer of the lung to have a continuously downhill course. I shall agree with the pathologist who said that there was no malignant disease.

Perhaps Dr. Holmes can help us by interpreting the x-ray films.

DR. GEORGE W. HOLMES: The first film was taken in the usual manner, and the second with a grid to bring out the bronchi and the shadows that show in the lateral view as described in the text. This is typical of collapse of the lung. We have all the signs, namely, decrease in size, increased density in the involved area, displacement of the mediastinal contents toward the affected side, limitation of the respiratory movements of the diaphragm on the affected side and increased brilliancy in the portion of the lung below the affected area. Of course, these are statements made by the one who interpreted the film, and we have to take that into consideration in deciding.

We see here that there is obvious dullness at the right apex. It is not mottled, nor has it the character that one expects to see with old tuberculosis. Then we see along here a dense line that represents the border of the septum, and that is much too high. One can be quite certain that the picture represents a retracted lung; whether that was due to the shutting off of air by something in the bronchus or to a fibrotic process in the lung itself is not too clear. I should think that if it had been due to fibrosis in the lung itself there would be more of the signs of fibrosis in the lung. To me, this looks much more like a collapsed than a fibrotic lung.

Dr. Beckman mentioned the possibility of adenoma. In practically all our cases of benign adenoma the lesion has occurred in one of the large bronchi, not in a small one. This lesion, if it is an obstructing lesion, is not in one of the large bronchi; it would have to involve the small bronchi to produce the appearance. Furthermore, we can see the large bronchi fairly well, and they show no evidence of tumor.

DR. BECKMAN: What about the areas that were supposed to be filled with air?

DR. HOLMES: I should take that statement with a grain of salt. They may or may not represent something. They were possibly areas of lung that were not collapsed.

DR. BECKMAN: That is at least helpful to me, because I feel more secure in the fact that there was real atelectasis. Can you tell whether it was atelectasis or fibrosis? Perhaps that is not a fair question.

DR. HOLMES: My opinion is that it was atelectasis and not fibrosis, but it is not based on a great deal of evidence.

DR. BECKMAN: It is perfectly possible that he had pulmonary fibrosis following pneumonia, although I do not believe that it is likely. I am more in favor of a lesion that occluded some of the bronchi. There are several. I do not know which are the most frequent, but certainly there are various tumors that can do that, and then there is the case¹ that Dr. Helen Pittman discussed here some months ago — a bronchial tuberculosis with a lesion sufficiently large to occlude a bronchus and produce atelectasis. I should think that would have to be seriously considered here.

There is no information on the examination of the sputum.

DR. RICHARD H. SWEET: The sputum was examined a number of times, not here, but elsewhere, and nothing was found.

DR. BECKMAN: I am afraid that I am not sufficiently expert in lung diseases to do anything but guess concerning the nature of this lesion. I am helped a little bit by the fact that an operation was performed. I do not believe that anyone would operate on a patient with pulmonary fibrosis if they were able to make that diagnosis. If I had been handling this case, I should have wanted a bronchoscopy. Possibly that is the operation noted in the record. If anything was learned, it means that the lesion was something that could be seen through the bronchoscope and could be biopsied. As I said before, I have to guess, but shall say that the patient had bronchial tuberculosis, which had occluded one or several bronchi and had produced atelectasis.

DR. J. H. MEANS: Dr. Beckman showed me the abstract of the history this morning. I was interested and looked up in Dr. Lord's book² to see what he had to say about lung conditions that

monary infarction would cover all this. People with pulmonary infarction not uncommonly have jaundice, a palpable liver, an increased pulmonic second sound and substernal pain. They also have shortness of breath at rest. One thing to back this up is that there was evidence of varicose veins, which are liable to thrombosis.

I believe that the absent pulsations of the dorsalis pedis arteries were associated with a general arteriosclerotic process. Combined systemic disease, to account for the loss of reflexes, is hardly borne out by a red-cell count of 4,200,000 and an adequate hemoglobin. Some rare condition of the peripheral nerves, such as beriberi or avitaminosis, seems improbable because of the patient's general appearance. He was only mildly dehydrated. A dissecting aneurysm could account for the absence of the dorsalis pedis pulsations. I am quite certain, however, that if he had had enough of a dissecting aneurysm to occlude the aorta from without, he would have been in shock and unable to maintain a blood pressure of 186 systolic, 120 diastolic. The only characteristic feature of a dissecting aneurysm in this case is the sudden pain in the back. I doubt that that is a cause of lost circulation.

We then come to the x-ray examination, which shows evidence of the fluid of congestive failure, increased lung markings, an enlarged heart and a tortuous and sclerotic aorta. The slightly elevated blood nonprotein nitrogen (45 mg. per 100 cc.) probably goes with a general process of decompensation. The electrocardiogram is interesting if we are considering a diagnosis of angina pectoris, because there is no evidence of coronary occlusion. They speak of sagging in the ST segments in Leads 1 and 2, which is usually considered to be due to digitalis, and of course, this patient had been taking digitalis. The total inversion of Lead 3 was probably due to a high diaphragm, and there was inversion of the T waves in Lead 3, and slight elevation of the ST segments. In fact, this tracing shows very deep T waves in Lead 3. It is difficult to determine how much actual left-axis deviation there is, even in view of the large size of the heart. In view of the total inversion I am not quite ready to think that this single electrocardiogram represents unequivocal evidence of coronary thrombosis.

Apparently the congestive heart failure increased and the patient began to cough up blood. More rales were heard, and it was noticed that the substernal distress, pain as well as shortness of breath, I presume, was relieved by sitting up. I believe that the diagnosis of hypertensive heart disease is justifiable. He had generalized arteriosclerosis, and he had angina pectoris. In addition he had pulmonary infarcts, varicose veins with thrombosis, and chronic cholecystitis and cholelithiasis, which would account for the occasional pain of thirty years' duration.

DR. CONGER WILLIAMS: I saw this patient on just one occasion. At that time I wondered whether

at least some of his discomfort might have been due to orthopnea, because the statement was made that his pain was much worse on lying down and relieved by sitting up. Although it did not seem likely that all the discomfort was the result of orthopnea, it appeared reasonable that some was due to that as a result of congestive failure. Presumably he was in failure at that time.

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CLINICAL DIAGNOSES

Myocardial infarction.
Pulmonary edema.

when he began to notice chest pain and shortness of breath on exertion, which were relieved by rest. The frequency of these attacks increased. About two weeks before entry, dyspnea and pain first appeared during rest, and in the few days before admission they became almost constant. The pain was substernal and radiated to the left shoulder and to the jaws and was accompanied by a cough.

One year before entry the patient had an unexplained fall, without loss of consciousness, fainting, weakness or visual disturbances preceding or following the fall. Since the age of thirty he had had occasional attacks of agonizing pain in the epigastrium during which he fell to the floor with paroxysms of pain. He could not tolerate fatty foods of any kind. He had not noted clay-colored stools, jaundice or changes in the urine.

Physical examination showed a dyspneic, somewhat icteric and mildly dehydrated man. The neck veins were prominent in a semireclining position. The lower thirds of both lung fields were slightly dull, and many rales were heard on auscultation. The left border of cardiac dullness was 12 cm. from the midline in the fifth space. The sounds were distant. There was reduplication of the second sound in both the aortic and mitral regions. The rate was regular, and there was no pulse deficit. The pulmonic second sound was greater than the aortic. A Grade II apical systolic murmur was heard. The liver edge was palpable one and a half fingerbreadths below the costal margin. Evidence of old varicose vein edema was seen in both lower legs. The dorsalis-pedis pulsations could not be felt. The knee and ankle jerks were absent. The tendon reflexes of the upper extremities were decreased.

The blood pressure was 186 systolic, 120 diastolic. The temperature was 100°F., the pulse 100, and the respirations 25 to 35.

Examination of the blood showed a red-cell count of 4,250,000, with 12.2 gm. of hemoglobin. The white-cell count was 16,600, with 82 per cent neutrophils. A blood Hinton test was negative. The urine was normal. The blood nonprotein nitrogen was 45.5 mg. per 100 cc.

An x-ray film of the chest showed enlargement of the heart in the region of the left ventricle. The transverse diameter of the heart was 16.7 cm., and the inner diameter of the chest 28.5 cm. A moderate amount of fluid was present in both pleural cavities. The hilar shadows were prominent, and the vascular markings were increased throughout both lungs. The aorta was tortuous but not dilated.

The patient was given 0.4 mg. of nitroglycerin, which relieved the pain. He was also given 100 mg. of Demerol intramuscularly and 6 cc. of Cedilanid subcutaneously, followed by 2 cc. in four hours, and he was placed on 0.1 gm. of digitalis daily. An electrocardiogram on the second hospital day showed normal rhythm, with a rate of 110. There was total inversion in Lead 3. The ST segments in Leads 1

and 2 were sagging. The T waves in Lead 3 showed late inversion; Lead 4 looked good.

The patient was unable to sleep or rest because of shortness of breath and substernal discomfort. The anginal pains were fairly well controlled by Demerol. He continued to cough and to raise a small amount of blood. The pulse remained rapid. On the fifth hospital day the lungs showed an increase in the moisture in the bases, and there was some pitting edema of the ankles. He was given 2 cc. of Mercupurin intravenously for two days. The substernal distress seemed to be relieved by sitting up, but his condition continued to fail, and he died on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. SYLVESTER MCGINN: No single diagnosis that I can think of seems adequate to cover everything in this case, and a number of the symptoms have to be analyzed separately.

First, I should like to speak of the dyspnea, the shortness of breath and pain in the chest coming on with exertion and, a short period of time after that, the shortness of breath at rest. There is no note whether this dyspnea at rest came on suddenly, or whether it occurred in paroxysms, such as cardiac asthma. Later on it is apparent that there was left ventricular weakness, and one might anticipate that there had been cardiac asthma. Then we come to the substernal pain on exertion, relieved by rest and nitroglycerin. Later the pain was constant and came when at rest. Immediately the anginal syndrome is suggested. This man was having midepigastric pain of some severity over a thirty-year period, which occasionally forced him to bend over and fall to the floor. When people assume the knee-chest position and have deep midepigastric pain one thinks of pancreatitis. Since the attacks were repeated, it is quite possible in this case that the patient had chronic cholecystitis with the passage of small calculi, giving biliary colic. We do not know how often these pains occurred, but that is the diagnosis that most adequately covers these attacks.

In the physical examination several features stand out. One thing is definite — the blood pressure of 186 systolic, 120 diastolic. Again, there is evidence that, by percussion, the heart was enlarged in the region of the left ventricle. Other evidence of right-heart strain is shown by increased fullness of the left cervical veins and the fact that the pulmonic second sound was greater than the aortic early, even though the patient had hypertension. We also find that the liver was palpable one and a half fingerbreadths below the costal margin and that there was a moderate grade of jaundice. There are several conditions that could cause acute or even chronic right-heart strain. I am assuming that something happened two weeks prior to entry that was a little different from the previous illness. Pul-

monary infarction would cover all this. People with pulmonary infarction not uncommonly have jaundice, a palpable liver, an increased pulmonic second sound and substernal pain. They also have shortness of breath at rest. One thing to back this up is that there was evidence of varicose veins, which were liable to thrombosis.

I believe that the absent pulsations of the dorsalis pedis arteries were associated with a general arteriosclerotic process. Combined systemic disease, to account for the loss of reflexes, is hardly borne out by a red-cell count of 4,200,000 and an adequate hemoglobin. Some rare condition of the peripheral nerves, such as beriberi or avitaminosis, seems improbable because of the patient's general appearance. He was only mildly dehydrated. A dissecting aneurysm could account for the absence of the dorsalis pedis pulsations. I am quite certain, however, that if he had had enough of a dissecting aneurysm to occlude the aorta from without, he would have been in shock and unable to maintain a blood pressure of 86 systolic, 120 diastolic. The only characteristic feature of a dissecting aneurysm in this case is the sudden pain in the back. I doubt that that is a cause of lost circulation.

We then come to the x-ray examination, which shows evidence of the fluid of congestive failure, increased lung markings, an enlarged heart and a tortuous and sclerotic aorta. The slightly elevated blood nonprotein nitrogen (45 mg. per 100 cc.) probably goes with a general process of decompensation. The electrocardiogram is interesting if we are considering a diagnosis of angina pectoris, because there is no evidence of coronary occlusion. They speak of sagging in the ST segments in Leads 1 and 2, which is usually considered to be due to digitalis, and of course, this patient had been taking digitalis. The total inversion of Lead 3 was probably due to a high diaphragm, and there was inversion of the T waves in Lead 3, and slight elevation of the ST segments. In fact, this tracing shows very deep T waves in Lead 3. It is difficult to determine how much actual left-axis deviation there is, even in view of the large size of the heart. In view of the total inversion I am not quite ready to think that this single electrocardiogram represents unequivocal evidence of coronary thrombosis.

Apparently the congestive heart failure increased and the patient began to cough up blood. More rales were heard, and it was noticed that the substernal distress, pain as well as shortness of breath, I presume, was relieved by sitting up. I believe that the diagnosis of hypertensive heart disease is justifiable. He had generalized arteriosclerosis, and he had angina pectoris. In addition he had pulmonary infarcts, varicose veins with thrombosis, and chronic cholecystitis and cholelithiasis, which would account for the occasional pain of thirty years' duration.

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at least some of his discomfort might have been due to orthopnea, because the statement was made that his pain was much worse on lying down and relieved by sitting up. Although it did not seem likely that all the discomfort was the result of orthopnea, it appeared reasonable that some was due to that as a result of congestive failure. Presumably he was in failure at that time.

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CLINICAL DIAGNOSES

Myocardial infarction.
Pulmonary edema.

DR. MCGINN'S DIAGNOSES

Hypertensive heart disease.
 Arteriosclerosis, generalized.
 Angina pectoris.
 Pulmonary infarcts.
 Thrombosis: leg veins.
 Chronic cholecystitis and cholelithiasis.

ANATOMICAL DIAGNOSES

Coronary thrombosis, recent, right.
 Myocardial infarction, recent: left ventricle.
 Pericarditis, acute, fibrinous.
 Cardiac hypertrophy, hypertensive type.
 Pulmonary edema and congestion.
 Hydrothorax, bilateral.
 Peripheral edema, slight.
 Arteriosclerosis, generalized.
 Cor pulmonale?
 Pulmonary atelectasis, bilateral.
 Esophageal varices.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed a heart weighing over 600 gm., with an enlarged left ventricle and a thick right ventricle, measuring 6 mm.

DR. WHITE: That would help to balance the electrical axis. In other words, it is possible that he had enough left ventricular failure to give him some right ventricular hypertrophy, or there may have been some other cause in the lungs.

DR. CASTLEMAN: The medium-sized arteries in the lungs were definitely hypertrophied, but there was no cause that we could find for that.

In the heart there was an extremely large posterior infarct involving the apex; this must have been quite recent because of a large number of polymorphonuclears within it, but organization was progressing.

DR. WHITE: How old was it? A few days, or older?

DR. CASTLEMAN: About two weeks.

DR. WHITE: It was probably present when he entered the hospital?

DR. CASTLEMAN: Yes. The cause of the infarction was a large thrombus of the right coronary artery, beginning about 5 cm. from the origin of the artery and measuring 6 cm. in length. It was one of the longest coronary thrombi that I have seen.

DR. WHITE: I suppose that with the progression of this infarct, one might have expected an inversion of T₂.

DR. CASTLEMAN: The gall bladder was normal. The lungs showed atelectasis in addition to moderate medial hypertrophy of the small arteries. I do not suppose that the process was extensive enough to call Ayerza's disease, but it probably accounted somewhat for the right ventricular hypertrophy.

DR. JONES: Was there any other evidence of previous thrombosis?

DR. CASTLEMAN: The coronary arteries showed extreme sclerosis, such as one sees in patients with angina.

DR. WHITE: Was there any explanation of the pain in the epigastrium?

DR. CASTLEMAN: No. We found nothing in the gastrointestinal tract except four or five varices in the lower end of the esophagus, with no cirrhosis, the cause of the varices was undetermined.

DR. JONES: That is impressive because it is rare to find so-called "congenital varices," or I suppose a better term is "varices, cause unknown." I do not believe that they would give symptoms. There was no difficulty in swallowing. That is an interesting anatomical finding without explanation. He did not have a hernia?

DR. CASTLEMAN: None that was apparent. Unless definitely looked for, however, a hiatus hernia can be easily overlooked.

He had acute pericarditis secondary to the infarction. Do you think that might affect the electrocardiogram, Dr. White?

DR. WHITE: There was not enough wrong in his one record to suspect it.

DR. McGinn brought up the matter of hypertension and that is one point to which attention should be called. The blood pressure often comes down during pain from acute myocardial infarction, but not infrequently the reverse is true, and occasionally we have seen a higher pressure than that at any other time, either before or after.

DR. JONES: How long does it persist after thrombosis has taken place—twenty-four to thirty-six hours?

DR. WHITE: It subsides in a few hours or in a day or two; but it is a point that may lead one astray if one always expects a drop in blood pressure in coronary thrombosis.

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THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

ANNUAL MEETING OF THE AMERICAN MEDICAL ASSOCIATION

AFTER an interval of two years the American Medical Association again held its annual meeting, this time in Chicago on June 12, 13, 14, 15 and 16. In spite of the difficulties of travel and anxieties at home the registration was about normal. The section meetings were, for the most part, crowded. The programs were varied and interesting. Although the scientific exhibit was perhaps not quite so large as usual, it maintained its usual standard.

The House of Delegates convened on Monday, with an attendance of 170 out of a possible 175. The secretary of the Association again reported an in-

crease in membership. There are now 124,452 members, against 122,741 in 1942. Deaths of members have increased, however, there having been 2019 during the year. About half these deaths were due to some form of cardiac disease and about half the cardiac deaths were caused by disease of the coronary arteries. This perhaps is an indication of the tempo at which civilian physicians are now working.

The House listened to reports of its officers, the Board of Trustees and the various councils and committees. The address of the president, James E. Paullin, should be read with care. It gives an idea of the vast amount of work being done by various unpaid committee members during these trying times, in spite of all they have to do in their own practices. His closing remarks were a plea for unity within the organization:

It is only by the development of complete unity and support that the views of the medical profession, which have been developed for the best interests of the public and for the advancement of science, can be made to prevail. If the purposes and ideals and desires for which we as a medical profession stand are worth while, then there should be the loyal support of every member of all organizations to see that they prevail.

Dr. Herman L. Kretschmer, president-elect, stressed the need of further education of the public regarding medical economics, particularly by general practitioners in their local communities.

Probably the most important action taken by the House of Delegates was the dispatch of a telegram to various authorities in Washington protesting the curtailment of the Specialized Army Training program as it pertains to premedical and medical students. This was considered to be the most serious situation confronting the medical profession today, since it is not possible to fill the enrollment of medical schools with women and physically disqualified men. If enough doctors to offset an approximate annual deficit of 2000 are to be obtained, some way to defer premedical students from the draft must be found.

Much was said about postwar planning. It was recommended that a central bureau be established in Chicago to provide information to physicians returning from service concerning internships, residencies, fellowships, postgraduate courses and so forth. It was stated that the experience gained

in the wartime graduate meetings that have been held so successfully in numerous military hospitals might provide a pattern for future postgraduate teaching.

The House was honored by the presence of Surgeon General Kirk of the Army Medical Corps, and of Surgeon General McIntire of the Navy Medical Corps, both of whom addressed the meeting and were enthusiastically received.

The climax for the Massachusetts delegation came, however, in the privilege of presenting Dr. Roger I. Lee's name for the office of president-elect. The enthusiasm with which the nomination was received and the prompt and unanimous election attest the high regard in which Dr. Lee is held by the House of Delegates. With ten years of service as a trustee, few men have come so well equipped for this exacting and important position. Again, Massachusetts has cause to rejoice.

THE OUTLOOK FOR MENINGOCOCCAL MENINGITIS

EPIDEMICS of meningococcal meningitis are known to occur irregularly in cycles, which usually last from two to five years. There are, in addition, secondary rises and falls in incidence, with peaks occurring during the fall and winter of each year within a large epidemic cycle. During the course of an epidemic a comparison of the incidence of the disease at any time of the year with its occurrence during the corresponding period of the preceding year may therefore give some clue whether the epidemic is waxing or waning, and in this way one may predict whether more or fewer cases are to be expected during the following year and even during the succeeding weeks and months.

A recent summary of the incidence of meningitis, which is included among the morbidity reports of notifiable diseases,¹ indicates that there were more cases during the year 1943 than in 1942. A total of 612,068 cases were reported during the former, and 546,023 cases during the latter. The provisional mortality figures for the first nine months of 1943 show more strikingly the increase in the disease that occurred during that period over the corresponding months of the two previous years.² The mortality in thirty-

eight states during 1943 was 2.0 per 100,000 population, as compared with 0.6 during 1942 and 0.5 during 1941. There were deviations from these figures in certain parts of the country, but the great majority of states had rates that were quite similar both qualitatively and quantitatively. Notable exceptions are Pennsylvania and Montana: in the former the mortalities were respectively two and a half and three and a half times as great in 1942 and 1943, and in the latter the 1943 figure was 8.0 deaths per 100,000 population, compared with 0.4 for each of the two previous years.

More recent figures, however, offer encouraging evidence that the epidemic is subsiding or at least is beginning to decline. In the morbidity report for the week ending March 11, 1944,³ the weekly incidence of meningococcal meningitis was lower than that for the corresponding week last year, this being the first time that a decline had been noted. Subsequent reports⁴ showed that the downward trend continued during four successive weeks, but during the week ending April 22, the incidence was slightly higher than in the previous year. Such slight irregularities are to be expected, owing to variations in the occurrence of the disease in different parts of the country, and do not necessarily interfere with the general trend of the epidemic incidence; in fact, the very next report⁵ indicated that the downward swing was continuing.

Although the epidemic appears to be subsiding, there will undoubtedly be appreciable numbers of cases of meningococcal meningitis during the coming fall and winter, with a peak that will be appreciably lower than that of the past year. Physicians must still be on the lookout for cases and must treat them early and adequately with sulfonamide drugs to keep the mortality at a minimum. One should also be on the lookout for cases of meningococcemia without meningitis, since such patients respond promptly to sulfonamide therapy and since early treatment usually forestalls meningitis and other focal complications, such as arthritis and endocarditis.

REFERENCES

1. *Pub. Health Rep.* 59:376, 1944.
2. *Ibid.* P. 594.
3. *Ibid.* P. 372.
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MASSACHUSETTS MEDICAL SOCIETY

THE BLUE SHIELD

While countless and voluminous opinions were expressed concerning legislative proposals for legalized medicine, the sponsors of the Blue Shield sought out the causes for such bills and attempted to neutralize them by more answerable methods.

The Blue Shield in Massachusetts now numbers nearly 35,000 members. Employee groups have been formed in 432 industrial and business organizations. Although more than 3300 Massachusetts doctors have become participating physicians, there are still many members of the profession who have not yet agreed to take an active part in the plan.

Some doctors object to having Blue Shield put a price on their services to the patient. These men should realize, however, that only the low-income subscriber is affected by the set fees, and as time goes on, 100 per cent collections obtainable through Blue Shield will create a better situation than higher fees and 50 to 80 per cent collections. Blue Shield subscribers in the upper-income brackets may be charged by the doctor with the difference between the amount specified in the fee schedule and his regular fee.

A few busy physicians fear that under Blue Shield they would have to serve many more patients than they have time for at present. Such fears are unfounded because Blue Shield guarantees the free choice of patients and in no manner does it insist on doctors taking Blue Shield subscribers as patients whom they would not ordinarily treat.

Several doctors state that they do not agree with the principles of a prepayment plan. This viewpoint is held by an extremely small minority, and is gradually changing to that of the leading physicians in the country, who realize that prepayment is the only answer to a better distribution of medical care. Such doctors may also remember that if the solution to the problem becomes impossible on a voluntary basis, the people themselves, who have already gone on record as desiring an easier method of paying their doctors' bills, will make decisions arbitrarily through legislation.

The Blue Shield is still in its infancy. Its growth has been satisfactory, but if the public demand is to be satisfied, the Blue Shield must receive the same whole-hearted support from physicians that the Blue Cross has obtained from its member hospitals. The latter is now adding members at the rate of a thousand a day.

If you are not yet a Blue Shield participating physician, you are urged to write to the Blue Shield office at 230 Congress Street, Boston 6, for further information.

DEATH

MOODY — Flora F. Moody, M.D., of Springfield, died June 26. She was in her seventy-fourth year.

Dr. Moody received her degree from Tufts College Medical School in 1898. She was a member of the American Medical Association and the Springfield Woman's Medical Club.

Her husband, a son, three sisters and a brother survive.

WAR ACTIVITIES

POSTWAR PLANNING

BUREAU OF MEDICAL EDUCATION CREATED BY NEW YORK ACADEMY OF MEDICINE

Anticipating an unprecedented demand for postgraduate medical education on the termination of war, particularly from physicians returning to civil life from service in the armed forces, and from civilian physicians from Central and South America, as well as from European countries released from Nazi control, the New York Academy of Medicine has created the Bureau of Medical Education.

The function of this bureau will be to serve all physicians interested in furthering their medical knowledge, but particularly physicians returning from the war, and the increasing numbers of foreign physicians who come to New York for postgraduate instruction and training. It will be organized by and operated under the supervision of the Committee on Medical Education of the New York Academy of Medicine and will render its services without charge. One of its chief functions will be to publish announcements of postgraduate medical courses conducted by the universities and the hospitals of New York City. Thirty-three of the leading hospitals have been invited to collaborate in this undertaking, and advisers representing the special fields of medical practice have been appointed to supervise the work of the bureau.

MISCELLANY

DEPARTMENT OF MEDICAL SCIENCES ESTABLISHED AT BROWN UNIVERSITY

The establishment of the Department of Medical Sciences at Brown University was recently announced by President Henry M. Wriston. This department will perform a number of important functions within the University and in the relations of the University to the medical profession and hospitals of the community. Charles A. McDonald, M.D., and Alex M. Burgess, M.D., physicians connected with the Division of University Health for some time, have been appointed professors of health and hygiene in this new department.

Dr. Wriston pointed out that through this department the University will assume a larger responsibility for the general education of its students in matters of health as a requisite of effective accomplishment in college and after-college years. He went on to say that special attention will be given to the orientation of students who are planning to enter the medical profession and that the department will offer facilities for advanced study and research, being designed in part to meet the needs and desires of recent graduates of medical schools whose postgraduate studies in certain specialized fields of medical science have been interrupted by war service. Dr. Wriston stated that opportunities for specialized study will also be available to other interested members of the medical profession, emphasizing that the University will be prepared to co-operate in the development of programs of postgraduate study and research for members of the resident staffs of the hospitals of the community.

CORRESPONDENCE

NEW POLICIES OF BOARD OF REGISTRATION IN MEDICINE

To the Editor: On May 17, 1944, the Board of Registration in Medicine voted unanimously that it shall be the policy of the Board, following a hearing, to revoke or suspend, as

in the wartime graduate meetings that have been held so successfully in numerous military hospitals might provide a pattern for future postgraduate teaching.

The House was honored by the presence of Surgeon General Kirk of the Army Medical Corps, and of Surgeon General McIntire of the Navy Medical Corps, both of whom addressed the meeting and were enthusiastically received.

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eight states during 1943 was 2.0 per 100,000 population, as compared with 0.6 during 1942 and 0.5 during 1941. There were deviations from the figures in certain parts of the country, but the great majority of states had rates that were quite similar both qualitatively and quantitatively. Notable exceptions are Pennsylvania and Montana: in the former the mortalities were respectively two and a half and three and a half times as great in 1943 and 1942 as in 1941, and in the latter the figure was 8.0 deaths per 100,000 population, compared with 0.4 for each of the two previous years.

More recent figures, however, offer encouraging evidence that the epidemic is subsiding or at least is beginning to decline. In the morbidity report for the week ending March 11, 1944,³ the weekly incidence of meningococcal meningitis was 1.5, less than that for the corresponding week last year, it being the first time that a decline had been noted. Subsequent reports⁴ showed that the downward trend continued during four successive weeks, and during the week ending April 22, the incidence was slightly higher than in the previous year. Slight irregularities are to be expected, owing to variations in the occurrence of the disease in different parts of the country, and do not necessarily interfere with the general trend of the epidemic incidence; in fact, the very next report⁵ indicates that the downward swing was continuing.

Although the epidemic appears to be subsiding there will undoubtedly be appreciable numbers of cases of meningococcal meningitis during the coming fall and winter, with a peak that will be appreciably lower than that of the past year. Physicians must still be on the lookout for cases and must treat them early and adequately with sulfonamide drugs to keep the mortality at a minimum. One should also be on the lookout for cases of meningococcal infection without meningitis, since such patients respond promptly to sulfonamide therapy and since early treatment usually forestalls meningitis and other focal complications, such as arthritis and endocarditis.

REFERENCES

1. *Pub. Health Rep.* 59:376, 1944
2. *Ibid.* P. 594
3. *Ibid.* P. 372.
4. *Ibid.* P. 558.
5. *Ibid.* P. 598

MASSACHUSETTS MEDICAL SOCIETY

THE BLUE SHIELD

While countless and voluminous opinions were expressed concerning legislative proposals for universalized medicine, the sponsors of the Blue Shield sought out the causes for such bills and attempted to neutralize them by more answerable methods.

The Blue Shield in Massachusetts now numbers nearly 35,000 members. Employee groups have been formed in 432 industrial and business organizations. Although more than 3300 Massachusetts doctors have become participating physicians, there are still many members of the profession who have not yet agreed to take an active part in the plan.

Some doctors object to having Blue Shield put a price on their services to the patient. These men should realize, however, that only the low-income subscriber is affected by the set fees. As time goes on, 100 per cent collections obtainable through Blue Shield will create a better situation than higher fees and 50 to 80 per cent collections. Blue Shield subscribers in the upper-income brackets may be charged by the doctor with the difference between the amount specified in the fee schedule and his regular fee.

A few busy physicians fear that under Blue Shield they would have to serve many more patients than they have time for at present. Such fears are unfounded because Blue Shield guarantees the free choice of patients and in no manner does it insist on doctors taking Blue Shield subscribers as patients whom they would not ordinarily treat.

Several doctors state that they do not agree with the principles of a prepayment plan. This viewpoint is held by an extremely small minority, and is gradually changing to that of the leading physicians in the country, who realize that prepayment is the only answer to a better distribution of medical care. Such doctors may also remember that if the solution to the problem becomes impossible on a voluntary basis, the people themselves, who have already gone on record as desiring an easier method of paying their doctors' bills, will make decisions arbitrarily through legislation.

The Blue Shield is still in its infancy. Its growth has been satisfactory, but if the public demand is to be satisfied, the Blue Shield must receive the same whole-hearted support from physicians that the Blue Cross has obtained from its member hospitals. The latter is now adding members at the rate of a thousand a day.

If you are not yet a Blue Shield participating physician, you are urged to write to the Blue Shield office at 230 Congress Street, Boston 6, for further information.

DEATH

MOODY — Flora F. Moody, M.D., of Springfield, died June 26. She was in her seventy-fourth year.

Dr. Moody received her degree from Tufts College Medical School in 1898. She was a member of the American Medical Association and the Springfield Woman's Medical Club.

Her husband, a son, three sisters and a brother survive.

WAR ACTIVITIES

POSTWAR PLANNING

BUREAU OF MEDICAL EDUCATION CREATED BY NEW YORK ACADEMY OF MEDICINE

Anticipating an unprecedented demand for postgraduate medical education on the termination of war, particularly from physicians returning to civil life from service in the armed forces, and from civilian physicians from Central and South America, as well as from European countries released from Nazi control, the New York Academy of Medicine has created the Bureau of Medical Education.

The function of this bureau will be to serve all physicians interested in furthering their medical knowledge, but particularly physicians returning from the war, and the increasing numbers of foreign physicians who come to New York for postgraduate instruction and training. It will be organized by and operated under the supervision of the Committee on Medical Education of the New York Academy of Medicine and will render its services without charge. One of its chief functions will be to publish announcements of postgraduate medical courses conducted by the universities and the hospitals of New York City. Thirty-three of the leading hospitals have been invited to collaborate in this undertaking, and advisers representing the special fields of medical practice have been appointed to supervise the work of the bureau.

MISCELLANY

DEPARTMENT OF MEDICAL SCIENCES ESTABLISHED AT BROWN UNIVERSITY

The establishment of the Department of Medical Sciences at Brown University was recently announced by President Henry M. Wriston. This department will perform a number of important functions within the University and in the relations of the University to the medical profession and hospitals of the community. Charles A. McDonald, M.D., and Alex M. Burgess, M.D., physicians connected with the Division of University Health for some time, have been appointed professors of health and hygiene in this new department.

Dr. Wriston pointed out that through this department the University will assume a larger responsibility for the general education of its students in matters of health as a requisite of effective accomplishment in college and after-college years. He went on to say that special attention will be given to the orientation of students who are planning to enter the medical profession and that the department will offer facilities for advanced study and research, being designed in part to meet the needs and desires of recent graduates of medical schools whose postgraduate studies in certain specialized fields of medical science have been interrupted by war service. Dr. Wriston stated that opportunities for specialized study will also be available to other interested members of the medical profession, emphasizing that the University will be prepared to co-operate in the development of programs of postgraduate study and research for members of the resident staffs of the hospitals of the community.

CORRESPONDENCE

NEW POLICIES OF BOARD OF REGISTRATION IN MEDICINE

To the Editor: On May 17, 1944, the Board of Registration in Medicine voted unanimously that it shall be the policy of the Board, following a hearing, to revoke or suspend, as

the case may be, the registration of any physician who has been sentenced to a penal institution.

On that date the Board also voted unanimously that it shall be the policy of the Board, following a hearing, to revoke or suspend, as the case may be, the registration of any physician who has been committed to and not yet discharged from a mental hospital.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A National Health Service. By Alice Bush, M.D.; J. McMur-ray Cole, M.D.; E. F. Fowler, M.D.; Elizabeth Hughes, M.D.; Howard Gaudin, M.D.; Selwyn Morris, M.D.; Bruce Mackenzie, M.D.; and Douglas Robb, M.D. 12°, paper, 108 pp. Wellington, New Zealand: Progressive Publishing Society, 1943. 2/6.

In this small pamphlet will be found a description of a plan for the National Health Service in New Zealand. Its practical application is worked out for Auckland City and its suburbs, detail being given in four appendices.

The Nature and Treatment of Mental Disorders. By Dom Thomas V. Moore, O.S.B., Ph.D., professor of psychology and psychiatry, Catholic University of America. With a foreword by Edward A. Strecker, M.D., professor of psychiatry, Graduate and Undergraduate Schools of Medicine, University of Pennsylvania, and consultant and chief of service, Institute of the Pennsylvania Hospital, Pennsylvania. 8°, cloth, 312 pp. New York: Grune and Stratton, 1943. \$4.00.

This is a new manual on clinical psychiatry in which emphasis is placed on treatment. The author has appended a classification and definition of clinical entities of psychiatry.

Manual of Fractures: Treatment by external skeletal fixation. By C. M. Shaar, M.D., captain, Medical Corps, United States Navy; and Frank P. Kreuz, Jr., M.D., lieutenant commander, Medical Corps, United States Navy. 8°, cloth, 300 pp., with 148 illustrations. Philadelphia: W. B. Saunders Company, 1943. \$3.00.

This manual describes fully the new treatment of external fixation of fractures, which is ideal for use at sea and in mobile hospitals where transportation of patients becomes necessary.

Elements of Medical Mycology. By Jacob H. Swartz, M.D., assistant professor of dermatology, Harvard Medical School and Postgraduate School, and dermatologist, Massachusetts General Hospital. With an introduction by Fred D. Weidman, M.D., professor of dermatological research, University of Pennsylvania. 8°, cloth, 179 pp., with 78 illustrations. New York: Grune and Stratton, 1943. \$4.50.

This small manual is designed to serve as a guide to the study of fungus diseases.

The Dysenteric Disorders: The diagnosis and treatment of dysentery, sprue, colitis and other diarrhoeas in general practice. By Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P., senior physician to the Hospital for Tropical Diseases and the Royal Albert Dock and Tilbury hospitals, consulting physician in tropical diseases to the Dreadnought Seamen's Hospital, London, director, Division of Clinical Tropical Medicine, London School of Hygiene and Tropical Medicine, consulting physician to the Colonial Office and Crown Agents to the Colonies, consultant in tropical medicine to the Admiralty and to the Royal Air Force, and Lumleian Lecturer, Royal College of Physicians, 1941. With an appendix by W. John Muggleton, M.S.M., F.I.M.L.T., technical assistant. Second edition. 8°, cloth, 629 pp.,

with 23 plates and 108 illustrations. Baltimore: The W and Wilkins Company, 1943. \$10.00.

The first edition of this book was printed in 1939, and the second edition has been called for by the necessity of including many advances in etiology, diagnosis and treatment that have become available since its first publication. No drastic alterations have been made in the arrangement of the book, but much new knowledge has been incorporated in its proper place throughout the various chapters. A new chapter on pellagra has been inserted, and the etiology of the sprue syndrome and its relation to steatorrhea. Discussion of the treatment of bacillary dysentery with sulfaguanidine has been included.

NOTICES

MEDICOLEGAL CONFERENCE AND SEMINAR

The Massachusetts Medico-Legal Society in conjunction with the medicolegal departments of Harvard, Boston University and Tufts medical schools has arranged for an annual day conference to be held at the Mallory Institute of Pathology, Boston City Hospital, on Wednesday, October 19, 1944. It will include lectures, demonstrations, and informal discussions concerning many subjects in legal medicine, particularly stressing some of the more recent procedures. The meeting will be open to any registered physician, law police official, senior medical student or other medical investigator who may be interested and care to register. A limit in number has been made. There will be no fee for registration. Although advance application is not essential it would be helpful to those arranging the conference. Notice of intention to attend be sent prior to October 1 to Dr. W. H. Watters, Department of Legal Medicine, Harvard Medical School, Boston 15.

The Harvard Medical School, Courses for Graduates, with the co-operation of the medical schools of Boston University and Tufts College, offers a seminar in legal medicine to occur the entire week of October 2 to 7, inclusive. It is planned particularly for medical examiners and coroners' physicians but will be open to any other suitable graduate of an approved medical school. The course will be practical rather than theoretical and will consist of autopsy demonstration technique and interpretation of laboratory tests, study of 1 day-by-day cases of a medical examiner, round-table conferences, and the many subjects now included in the wide field of legal medicine. In order that each participant may receive the maximum benefit, the enrollment has been limited to fifteen. For the seminar the fee is \$25. Application should be made on or before October 1 to Harvard Medical School, Courses for Graduates, 25 Shattuck Street, Boston 15.

NEW YORK INSTITUTE OF CLINICAL ORAL PATHOLOGY

The New York Institute of Clinical Oral Pathology announces its first open meeting, to be held at the New York Academy of Medicine on Monday evening, October 30, Hosack Hall. Outstanding investigators will participate in a symposium "Fluorine and Dental Caries."

Members of the medical, dental, public-health and other professional groups are cordially invited. For further information all communications should be addressed to Roistacher, Executive Secretary, 101 East 79th Street, New York 21, New York.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 27

MONDAY, JULY 31

*12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, AUGUST 1

*12:15-1:15 p.m. Clinicoröntgenological conference. Peter Bent Brigham Hospital.

(Continued on page xiii)

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INFECTIOUS MONONUCLEOSIS SIMULATING BRUCELLOSIS*

A. DANIEL RUBENSTEIN, M.D., M.P.H.,† AND CAROLYN I. SHAW, Sc.B.‡

BOSTON

ALTHOUGH clinical and laboratory methods for the recognition of both infectious mononucleosis and brucellosis are reasonably adequate, differential diagnosis of these infections at times is subject to considerable confusion. Brucellosis, a bacterial disease, and mononucleosis, probably caused by a virus,¹ nevertheless present such similarities in their manifestations that one may readily be mistaken for the other.

In both diseases, fever of undetermined origin is usually the keynote of the clinical course. The presence of sore throat, lymphadenopathy and splenic enlargement suggests a diagnosis of infectious mononucleosis, which may be confirmed by blood studies and the heterophile antibody reaction. Except perhaps for varying degrees of leukopenia, most cases of undulant fever present no significant physical findings. The blood agglutination test is the one most frequently employed to corroborate the clinical impression. Unfortunately, isolation of the etiologic agent from the blood stream, the most reliable diagnostic aid, is not always successful. This is particularly true of infections caused by *Brucella abortus*.

Investigation of cases of undulant fever reported to the Massachusetts Department of Public Health has demonstrated at times a readiness to accept the agglutination reaction as the ultimate criterion in the diagnosis of this disease. It must, however, be borne in mind that a positive test may be indicative either of present infection or of previous exposure to the causative agent. Menefee and Johnston² have shown that a high titer of agglutinins may be demonstrated in the serums of patients with febrile diseases other than brucellosis.

In our experience, careful study of cases with positive agglutination reactions for undulant fever has occasionally revealed some other disease as the cause of an obscure hyperpyrexia. Recently a diagnosis of infectious mononucleosis was established in several such cases. With awareness of the similarity between these infections, it became

apparent that a certain percentage of cases suspected of being undulant fever might easily turn out to be infectious mononucleosis. Accordingly, it was decided to perform the heterophile antibody reaction routinely on a series of 1000 consecutive blood serums submitted by physicians to the State Bacteriological Laboratory for undulant-fever agglutination tests.

In each case in which a positive sheep-cell agglutination was elicited, the physician was interviewed to obtain additional laboratory and clinical data. If white-cell counts and blood smears were not already available, it was suggested that these examinations be made. In the cases in which the titer was less than 1:128, a second specimen was requested to ascertain the titer later in the course of the illness.

LABORATORY OBSERVATIONS

The number of specimens tested each month from May through October, 1943, and the number of positive sheep-cell and *Br. abortus* agglutinations are shown in Table 1. Each positive test represents

TABLE 1. Heterophile Antibody Reaction in Blood Serums Submitted for Undulant-Fever Agglutination Tests.

MONTH	NO. OF SERUMS TESTED	NO. OF POSITIVE HETEROPHILE ANTIBODY REACTIONS (1:128 or higher)	NO. OF POSITIVE UNDULANT-FEVER AGGLUTINATION TESTS (1:405 or higher)
May	108	2	7
June	212	3	9
July	219	0	6
August	159	4	4
September	144	0	5
October	158	4	5
Totals	1000	13	36

a final diagnosis of either undulant fever or infectious mononucleosis. All tests on questionable cases have been omitted. In the 1000 specimens, infectious mononucleosis was revealed in 13. In only 2 of these cases had this diagnosis been suspected by the physician who submitted the specimen; in other words, in 11 cases, this diagnosis might not otherwise have been revealed. It must be pointed out that a large proportion of the original

*From the Division of Communicable Diseases, Massachusetts Department of Public Health.

†District health officer, Massachusetts Department of Public Health.

‡Junior bacteriologist, Massachusetts Department of Public Health.

specimens were from patients with symptoms of long duration, the physician evidently having considered a diagnosis of chronic brucellosis. Since infectious mononucleosis is usually an acute, comparatively brief febrile illness, it was scarcely expected to find positive heterophile reactions among this group of cases. If these chronic infections had been excluded, the percentage of cases of infectious mononucleosis would have been appreciably greater.

This test series revealed only 36 cases of brucellosis. Since these specimens had been submitted specifically for undulant fever, the discovery of 13 cases of infectious mononucleosis represents by comparison a fairly high yield.

The cases of infectious mononucleosis are summarized in Table 2. In 2 cases (Cases 1 and 3), an

For this reason the total number of lymphocytes and monocytes was expressed as a percentage the mononuclear cells (Table 2), which varied from 50 to 90 per cent (considering only the highest percentage in each case). The known duration of fever varied from ten to twenty-three days. Cervical adenopathy was encountered in 7 cases, cervical lymphadenopathy in 10, and enlargement of the spleen in

EPIDEMIOLOGIC OBSERVATIONS

Brucellosis

The diagnosis of infectious mononucleosis rests on criteria that are fairly clearly defined. This is true of brucellosis unless the blood culture is positive. In contrast to the ambiguity associated with

TABLE 2. Summary of Laboratory and Physical Findings in 13 Cases of Infectious Mononucleosis

PATIENT	AGE	SEX	TITER OF SERUM	WHITE-CELL COUNT	PERCENTAGE OF MONONUCLEARS	SORE THROAT	ADENOPATHY	SPLenic ENLARGEMENT	DURATION OF FEVER
				$\times 10^3$					days
I M	21	I	1:64 1:1024	4.7 (Aug 17) 16.5 (Aug 21)	55 77	—	Cervical	+	15
A G	14	F	1:128	6.8	65	+	Cervical and inguinal	+	25
R N	28	M	1:64 1:256	7.2	52	—	None	—	21
R B	30	M	1:1024	7.8	55	+	Posterior cervical	—	17
E C	22	F	1:2048	14.0	55	+	None	—	10
R J	40	M	1:2048	10.6 (May 12) 13.7 (May 17) 15.1 (May 19)	67 71 70	+	None	—	18
H L	30	M	1:1024		50	+	Posterior cervical	—	18
D B	25	M	1:128	6.5 (Sept 17) 18.0 (Sept 27) 8.6 (Oct 18)	42 80 52		Posterior cervical	+	12
M B	20	I	1:1024	21.5	54		Posterior cervical	—	
L C	12	F	1:256	20.0 (Sept 9) 23.0 (Sept 17)	68	+	Cervical	—	10
L B	—	F	1:32,768	9.0	76	+	Cervical	—	9
N B	18	F	1:256	14.0	54		Posterior cervical	—	21
L L	34	M	1:512	16.3 (Oct 7) 22.9 (Oct 14) 22.1 (Oct 21)	74 77 78		Posterior cervical	—	14

initial test positive in a dilution of 1:64 rose to a higher titer in a subsequent specimen — 1:1024 in one case and 1:256 in the other. The highest titer obtained was 1:32,768, and 2 cases demonstrated positive reactions in a serum dilution of 1:2048. It is apparent that a titer of 1:64 is fair evidence of infectious mononucleosis. One case positive in this dilution (not included in Table 2), however, did not prove to be infectious mononucleosis.

White-cell counts were made in 12 cases and blood smears were examined in 13. The former ranged from 7200 to 23,000 (considering only the highest count in each case). Since the blood smears were performed in many laboratories, no conclusion could be drawn concerning specific blood cells.

its clinical manifestations, the epidemiology of undulant fever has been fairly definitely established.

Brucellosis is acquired by ingestion of infected dairy products or by contact with infected animals. In rare cases water has been incriminated as source.³ It has been observed that when a report of undulant fever cannot be traced either to raw milk or to potentially infected animals, review of the clinical findings may result in a change of diagnosis. In this manner epidemiologic investigations may become helpful in the diagnosis of undulant fever.

In Table 3 are summarized the sources of infection in 32 cases of undulant fever occurring in an urban state health district (North Metropolitan

strict). Of 18 cases traced to raw milk, 16 were traced by persons traveling outside this district. As a matter of fact, the amount of unpasteurized milk sold in this area is exceedingly small. Only 2 patients became infected from raw milk acquired within it.

On the other hand, out of 14 cases contracted within the area, 12 were traced to contact with humans or animal products, the infection having been acquired as a result of occupational exposure.

TABLE 3. *Sources of Infection in Cases of Undulant Fever Occurring in an Urban District (1930-1943).*

SOURCE	No. OF CASES
From milk	16
Outside district	2
Within district	7
Direct contact with animals	5
Indirect contact with animals or animal products	2
Unknown	2
Total	32

Direct contact with animals or animal carcasses by farmers, veterinarians or packing-house employees counted for 7 of these cases. Three patients were machinists in rendering plants and 2 were metal workers in packing houses. In each of these 5 cases the worker had handled machinery or other materials used in the processing of meat products, but no story of direct contact with animals or animal products could be elicited. All 5 cases occurred in plants where the attack rates for undulant fever among employees constantly handling carcasses or meat products were exceedingly low. Purriel et al.⁴ have found positive skin reactions for brucellosis among a large proportion of employees handling animal carcasses. It may be postulated that many of these workers develop immunity through long-continued exposure to the infectious agent. On the other hand, employees such as machinists, rarely in contact with the causative organisms, are more susceptible to a single chance exposure.

Infectious Mononucleosis

Since the etiology of infectious mononucleosis is not yet known, information concerning its epidemiology has been slowly accumulated. Since 1926, there has been a great deal of speculation concerning the possible etiologic relation of organisms of the genus *Listerella* to infectious mononucleosis in human beings.⁵ Janeway and Dammin⁶ investigated this question in 1941 by studying in patients with infectious mononucleosis the development of agglutinins against either of the two known groups of *Listerella*. Their observations suggested no relation between infectious mononucleosis and *Listerella* organisms.

Recently, Nettleship¹ recovered a virus from the blood and nasal washings of patients with infectious mononucleosis by inoculating sterile Berkefeld filtrates into the chorioallantoic membrane of the

chick embryo. Van den Berghe and Liessens^{7, 8} also considered the causative agent to be a virus, which they obtained in tissue culture. They reproduced the disease in monkeys, which later showed the typical blood picture and heterophile reaction.

Bernstein⁹ in an excellent review of the literature on infectious mononucleosis states that cases have been reported from all parts of the world. The disease occurs both sporadically and in epidemics. Outbreaks have taken place in schools^{10, 11} and in the general community.¹² The disease is well known to college physicians everywhere. With the exception of outbreaks in the Army,¹³ epidemics have not been found in any group above college age. During an outbreak, the resistance to the disease of persons in the older age groups may be quite striking.¹¹ It is well known that infectious mononucleosis is largely a disease of children and young adults. With the exception of a patient forty years old, all our patients were between the ages of twelve and thirty-four. Davis¹⁴ described an epidemic in an infants' ward.

Sporadic cases have been encountered during every month of the year. In a reported series⁹ the greatest incidence occurred in October. In some epidemics the attack rates are apparently quite high, but sporadic cases rarely give rise to secondary infections. Most hospitals admit cases of infectious mononucleosis to the open ward.

Of the 6 cases reported below, Cases 1 and 3 demonstrate the marked similarity between infectious mononucleosis and undulant fever. In each of the others an unusual feature of one or the other of these infections is described.

CASE REPORTS

CASE 1. D. B., a 25-year-old medical student, consulted his physician because of severe headache, prostration and intermittent fever. He had been well until September 14, 1943, when there was onset of headache and malaise. He felt feverish, and his temperature was 99.5°F. He was unusually tired and later developed a moderate degree of prostration. The past history was unimportant.

Physical examination was essentially negative throughout the first week of illness. The red-cell count was 4,490,000 and the hemoglobin 90 per cent. The white-cell count ranged from 6500 on September 17 to 18,000 on September 27, with differential counts as follows: on September 17, 57 per cent neutrophils, 35 per cent lymphocytes, 7 per cent monocytes and 1 per cent basophils; on September 27, 20 per cent neutrophils, 77 per cent lymphocytes and 3 per cent monocytes. Agglutination reactions for undulant fever and typhus fever were negative. On September 22, the Widal reaction was weakly positive in a dilution of 1:40. On the same day the heterophile antibody reaction was positive in a titer of 1:128. A stool culture on September 27 was negative for the typhoid bacillus. Urinalysis was negative.

The severe headache was a particularly troublesome symptom, although large doses of aspirin gave some relief. Sulfadiazine was administered for 4 days without any apparent response. Postcervical lymphadenopathy was noted on the 9th day of the illness, when the temperature had become practically normal. At the same time the spleen became palpable. The temperature was 99.8°F on September 25, and became normal thereafter. Except for a feeling of tiredness that persisted for 1 month, recovery was uneventful.

Diagnosis: infectious mononucleosis.

CASE 2. R. B., a 30-year-old machinist, was admitted to a hospital on May 25, 1943, with chief complaints of severe headache and fever. Except for an eruption in the region of both ankles he had been well until May 20, when he developed sore throat and fever. He believed that his symptoms were related to the rash on the ankles. Several days later he began having severe headaches. When the temperature and sore throat persisted, hospitalization was advised. The past history was not important except that the patient's legs were constantly exposed to cutting oils absorbed by his trousers.

On admission the temperature was 101°F. Except for an eruption on both ankles, the physical examination was not remarkable. The red-cell count was 4,600,000, the hemoglobin 87 per cent, and the white-cell count 7800, with 45 per cent neutrophils and 55 per cent lymphocytes. A blood culture on June 2 was negative. Urinalysis was negative. The agglutination tests on June 5 were as follows: typhoid and undulant-fever reactions, negative; heterophile antibody reaction, positive in a titer of 1:1024.

Until June 6 the temperature ranged from 98.8 to 103°F. The sore throat became worse following admission and the headaches were unusually severe. Occasionally there were chills and profuse sweats. On May 31, the lesions on the legs had healed completely but the headache persisted. On the same day there occurred several momentary faints. Lumbar puncture, performed because of the severe headache, backache and faints, revealed a clear, colorless fluid, with an initial pressure equivalent to 580 mm. of water, a cell count of 12 lymphocytes, a total protein of 57 mg. per 100 cc., a positive Pandy reaction and a normal sugar level. Following this lumbar puncture there was marked relief from symptoms. The temperature subsided within a few days, and the patient made an uneventful recovery. On June 1, enlargement of the posterior cervical lymph nodes was discovered.

Diagnosis: infectious mononucleosis and occupational dermatitis of both ankles.

CASE 3. L. L., a 34-year-old married man, was admitted to a hospital on October 7, 1943, with a chief complaint of severe abdominal cramps. He had been well until three days prior to admission, when there were intermittent attacks of severe, cramplike pain in the lower abdomen, during which the patient felt nauseated but did not vomit. There were no other intestinal symptoms. When the attacks had persisted for 3 days, hospitalization was advised for further study. There was no history of any similar illness in the past.

On admission the temperature was 98.8°F., the pulse 90, and the respirations 20. Except for tenderness over the lower abdomen, the general physical examination was negative. The red-cell count was 4,900,000 and the hemoglobin 92 per cent. The white-cell count ranged from 16,300 on October 7 to 22,900 on October 14, with differential counts as follows: on October 7, 26 per cent neutrophils, 67 per cent small lymphocytes and 7 per cent large lymphocytes; on October 14, 23 per cent neutrophils, 52 per cent small lymphocytes and 25 per cent large lymphocytes; on October 21, 22 per cent neutrophils, 60 per cent small lymphocytes and 18 per cent large lymphocytes. Agglutination reactions using typhoid and brucella organisms were negative on October 8 and 9. The heterophile antibody reaction on October 9 was positive in a titer of 1:512. Urinalysis was negative.

The abdominal cramps persisted for 48 hours after admission and subsided with symptomatic treatment. On the 2nd hospital day, the temperature began to rise and the patient developed a low-grade fever that persisted for two weeks, the temperature ranging from 98.8 to 100°F. During that time he lost considerable strength and felt extremely tired. On the 8th day, enlargement of the left posterior cervical nodes was noted, and the swelling persisted throughout the hospital stay. The patient was discharged on the 18th day after having been afebrile for 3 days. The feeling of tiredness persisted for several weeks after discharge.

Diagnosis: infectious mononucleosis.

CASE 4. J. O., a 44-year-old sheet-metal worker, was admitted to a hospital on March 28, 1943, with chief complaints of fever and malaise. He had been fairly well until March 21, when there was onset of malaise and anorexia. He tempted self-medication with proprietary drugs and bed rest, but without relief. He then became aware of chills, sweats and afternoon sweats. Within the next few days he began having severe occipital headaches. He consulted

his physician, who found that the temperature was 101°F. There was no cough or other symptoms of upper respiratory infection. The past history was not important except that the patient was employed as a sheet-metal worker in a painting plant. Although he did not handle meat products, he often repaired metal runways used in the processing of products.

On admission, the temperature was 101°F., the pulse 100, and the respirations 20. Physical examination was negative. The red-cell count was 4,200,000, the hemoglobin 81 per cent, and the white-cell count 10,400, with 76 per cent neutrophils, 23 per cent lymphocytes and 1 per cent eosinophils. Urinalysis was negative. A blood Hinton test was negative. Agglutination tests on April 2 were reported as follows: typhoid and paratyphoid reactions, negative; undulant-fever reaction, positive in a titer of 1:405. X-ray examination of the chest on April 2 was negative.

The temperature remained elevated for 3 weeks after admission. During the 1st week it averaged 101°F. during the afternoon and evening and was considerably lower in the morning. During the 2nd and 3rd weeks the patient was afebrile in the morning, and the afternoon and evening temperatures varied from 99.6 to 102°F. There was change in the physical findings. Recovery was uneven following subsidence of the fever.

Diagnosis: undulant fever.

CASE 5. R. L., a 5-year-old boy, was admitted to a hospital on April 3, 1935, with chief complaints of fever and malaise. He had been well until 8 days prior to admission, when he became listless and fretful. There was general malaise and anorexia. The family physician found that the rectal temperature was elevated, varying between 99 and 103°F. Since there was no improvement after 4 days, hospitalization was advised. The past history revealed the usual childhood diseases. For several months the patient had been drinking raw milk. Adjoining the property on which he lived, there was a large piggery, but no history of contact with pigs could be established.

On admission on January 25, the temperature was 105°F., the pulse 120, and the respirations 36. The patient appeared pale and listless and was quite ill. The significant findings of the physical examination were marked splenomegaly, hepatomegaly and engorgement of the superficial vessels of the abdomen. The red-cell count was 3,640,000 and the hemoglobin 78 per cent. The white-cell count gradually rose from 3400 on January 21 to 5500 on February 27, with differential counts as follows: on January 21, 46 per cent neutrophils, 46 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils; on January 27, 36 per cent neutrophils, 52 per cent lymphocytes, 10 per cent monocytes and 2 per cent basophils; on February 3, 44 per cent neutrophils, 44 per cent lymphocytes and 5 per cent monocytes. Urinalysis was essentially negative. A blood Hinton test was negative. Agglutination tests on January 23 were as follows: typhoid and typhus reactions, negative; undulant-fever reaction positive in a dilution of 1:32,805 and partially positive one of 1:98,415. On February 15 and February 20, blood cultures revealed *Br. suis*. On January 21, x-ray examination of the chest was negative.

The temperature remained extremely high during the first 2 weeks of the illness. On January 28, therapy with a brucella vaccine was instituted, and there was a marked rise in temperature following each dose. On February 7, there was some diminution in the size of the liver and spleen, although the patient still appeared quite ill. Late in February, except for the febrile response following the administration of vaccine, the temperature became normal. Later, when the vaccine was discontinued, the temperature remained normal. On March 12, there was a recurrence of fever, and this persisted until March 20. Thereafter, except for an occasional rise to 100°F. during the afternoon and evening, the patient remained afebrile. There was an uneventful recovery.

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The swelling subsided after 7 days, only to recur during the following week, when it lasted for 3 days. The temperature remained elevated for 2 weeks. Thereafter, although there was no recurrence of acute symptoms, the patient tired easily and was unable to exert himself as much as previously. This condition persisted for several months. In March, 1940, the agglutination reaction for undulant fever was positive in a dilution of 1:405. There had been some improvement in the patient's condition, but he had not recovered all his former vitality.

Diagnosis: undulant fever, with epididymitis.

DISCUSSION

Case 1 is presented as a typical example of infectious mononucleosis. Except for the absence of sore throat, which is a fairly common finding, the symptomatology and clinical course are characteristic. Headache is a frequent complaint. In Case 2, the severe persistent headache, faints and spinal-fluid findings suggested involvement of the central nervous system.

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Case 4 is an example of the usual clinical variety of undulant fever prevalent in Massachusetts. Most of the cases are extremely mild. Characteristically, the patient feels fairly well in the morning, and as the fever rises in the afternoon and evening the symptoms become more marked. The physical findings are usually insignificant.

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recurrences of fever with quiescent intervals. Such recurrences, however, are found only in the exceptional case. Most patients exhibit a single bout of fever lasting from a few days to several weeks or months, following which recovery is uneventful.

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Five cases of undulant fever occurred among machinists and metal workers handling materials

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On admission the temperature was 101°F. Except for an eruption on both ankles, the physical examination was not remarkable. The red-cell count was 4,600,000, the hemoglobin 87 per cent, and the white-cell count 7800, with 45 per cent neutrophils and 55 per cent lymphocytes. A blood culture on June 2 was negative. Urinalysis was negative. The agglutination tests on June 5 were as follows: typhoid and undulant-fever reactions, negative; heterophile antibody reaction, positive in a titer of 1:1024.

Until June 6 the temperature ranged from 98.8 to 103°F. The sore throat became worse following admission and the headaches were unusually severe. Occasionally there were chills and profuse sweats. On May 31, the lesions on the legs had healed completely but the headache persisted. On the same day there occurred several momentary faints. Lumbar puncture, performed because of the severe headache, backache and faints, revealed a clear, colorless fluid, with an initial pressure equivalent to 580 mm. of water, a cell count of 12 lymphocytes, a total protein of 57 mg. per 100 cc., a positive Pandy reaction and a normal sugar level. Following this lumbar puncture there was marked relief from symptoms. The temperature subsided within a few days, and the patient made an uneventful recovery. On June 1, enlargement of the posterior cervical lymph nodes was discovered.

Diagnosis: infectious mononucleosis and occupational dermatitis of both ankles.

CASE 3. L. L., a 34-year-old married man, was admitted to a hospital on October 7, 1943, with a chief complaint of severe abdominal cramps. He had been well until three days prior to admission, when there were intermittent attacks of severe, cramplike pain in the lower abdomen, during which the patient felt nauseated but did not vomit. There were no other intestinal symptoms. When the attacks had persisted for 3 days, hospitalization was advised for further study. There was no history of any similar illness in the past.

On admission the temperature was 98.8°F., the pulse 90, and the respirations 20. Except for tenderness over the lower abdomen, the general physical examination was negative. The red-cell count was 4,900,000 and the hemoglobin 92 per cent. The white-cell count ranged from 16,300 on October 7 to 22,900 on October 14, with differential counts as follows: on October 7, 26 per cent neutrophils, 67 per cent small lymphocytes and 7 per cent large lymphocytes; on October 14, 23 per cent neutrophils, 52 per cent small lymphocytes and 25 per cent large lymphocytes; on October 21, 22 per cent neutrophils, 60 per cent small lymphocytes and 18 per cent large lymphocytes. Agglutination reactions using typhoid and brucella organisms were negative on October 8 and 9. The heterophile antibody reaction on October 9 was positive in a titer of 1:512. Urinalysis was negative.

The abdominal cramps persisted for 48 hours after admission and subsided with symptomatic treatment. On the 2nd hospital day, the temperature began to rise and the patient developed a low-grade fever that persisted for two weeks, the temperature ranging from 98.8 to 100°F. During that time he lost considerable strength and felt extremely tired. On the 8th day, enlargement of the left posterior cervical nodes was noted, and the swelling persisted throughout the hospital stay. The patient was discharged on the 18th day after having been afebrile for 3 days. The feeling of tiredness persisted for several weeks after discharge.

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CASE 4. J. O., a 44-year-old sheet-metal worker, was admitted to a hospital on March 28, 1943, with chief complaints of fever and malaise. He had been fairly well until March 21, when there was onset of malaise and anorexia. He tempted self-medication with proprietary drugs and bed rest, but without relief. He then became aware of chilly sensations and afternoon sweats. Within the next few days he began having severe occipital headaches. He consulted

his physician, who found that the temperature was 101°F. There was no cough or other symptoms of upper respiratory infection. The past history was not important except that the patient was employed as a sheet-metal worker in a firing plant. Although he did not handle meat products, often repaired metal runways used in the processing of products.

On admission, the temperature was 101°F., the pulse and the respirations 20. Physical examination was negative. The red-cell count was 4,200,000, the hemoglobin 81 per cent, and the white-cell count 10,400, with 76 per cent neutrophils, 23 per cent lymphocytes and 1 per cent eosinophils. Urinalysis was negative. A blood Hinton test was negative. Agglutination tests on April 2 were reported as follows: typhoid and paratyphoid reactions, negative; undulant-fever reaction, positive in a titer of 1:405. X-ray examination of the chest on April 2 was negative.

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Diagnosis: undulant fever.

CASE 5. R. L., a 5-year-old boy, was admitted to a hospital on April 3, 1935, with chief complaints of fever and malaise. He had been well until 8 days prior to admission, when he became listless and fretful. There was general malaise, anorexia. The family physician found that the rectal temperature was elevated, varying between 99 and 103°F. Since there was no improvement after 4 days, hospitalization was advised. The past history revealed the usual childhood diseases. For several months the patient had been drinking raw milk. Adjoining the property on which he lived, there was a large piggery, but no history of contact with pigs could be established.

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Although some cases of infectious mononucleosis and undulant fever are striking in their manifestations, comparison of Case 1 and Case 4, each characteristic of the usually encountered clinical variety of the respective disease, demonstrates their marked similarity. Since infectious mononucleosis is not a reportable disease, no figures concerning its incidence are available. Our experience suggests, however, that it is a fairly common infection of young adults. For this reason, an awareness of the possibility of confusing these infections may prevent many errors in diagnosis.

SUMMARY

Experience with reported cases of undulant fever has demonstrated that this disease may be readily confused with infectious mononucleosis.

The heterophile antibody reaction, performed routinely on 1000 consecutive blood serums submitted by physicians for undulant fever agglutination, revealed 13 cases of infectious mononucleosis. Although these specimens were submitted specifically for undulant fever, only 36 were positive for that disease.

In urban areas, except for cases contracted elsewhere, undulant fever is essentially an occupational disease.

Five cases of undulant fever occurred among machinists and metal workers handling materials

CASE 2. R. B., a 30-year-old machinist, was admitted to a hospital on May 25, 1943, with chief complaints of severe headache and fever. Except for an eruption in the region of both ankles he had been well until May 20, when he developed sore throat and fever. He believed that his symptoms were related to the rash on the ankles. Several days later he began having severe headaches. When the temperature and sore throat persisted, hospitalization was advised. The past history was not important except that the patient's legs were constantly exposed to cutting oils absorbed by his trousers.

On admission the temperature was 101°F. Except for an eruption on both ankles, the physical examination was not remarkable. The red-cell count was 4,600,000, the hemoglobin 87 per cent, and the white-cell count 7800, with 45 per cent neutrophils and 55 per cent lymphocytes. A blood culture on June 2 was negative. Urinalysis was negative. The agglutination tests on June 5 were as follows: typhoid and undulant-fever reactions, negative; heterophile antibody reaction, positive in a titer of 1:1024.

Until June 6 the temperature ranged from 98.8 to 103°F. The sore throat became worse following admission and the headaches were unusually severe. Occasionally there were chills and profuse sweats. On May 31, the lesions on the legs had healed completely but the headache persisted. On the same day there occurred several momentary faints. Lumbar puncture, performed because of the severe headache, backache and faints, revealed a clear, colorless fluid, with an initial pressure equivalent to 580 mm. of water, a cell count of 12 lymphocytes, a total protein of 57 mg. per 100 cc., a positive Pandy reaction and a normal sugar level. Following this lumbar puncture there was marked relief from symptoms. The temperature subsided within a few days, and the patient made an uneventful recovery. On June 1, enlargement of the posterior cervical lymph nodes was discovered.

Diagnosis: infectious mononucleosis and occupational dermatitis of both ankles.

CASE 3. L. L., a 34-year-old married man, was admitted to a hospital on October 7, 1943, with a chief complaint of severe abdominal cramps. He had been well until three days prior to admission, when there were intermittent attacks of severe, cramplike pain in the lower abdomen, during which the patient felt nauseated but did not vomit. There were no other intestinal symptoms. When the attacks had persisted for 3 days, hospitalization was advised for further study. There was no history of any similar illness in the past.

On admission the temperature was 98.8°F., the pulse 90, and the respirations 20. Except for tenderness over the lower abdomen, the general physical examination was negative. The red-cell count was 4,900,000 and the hemoglobin 92 per cent. The white-cell count ranged from 16,300 on October 7 to 22,900 on October 14, with differential counts as follows: on October 7, 26 per cent neutrophils, 67 per cent small lymphocytes and 7 per cent large lymphocytes; on October 14, 23 per cent neutrophils, 52 per cent small lymphocytes and 25 per cent large lymphocytes; on October 21, 22 per cent neutrophils, 60 per cent small lymphocytes and 18 per cent large lymphocytes. Agglutination reactions using typhoid and brucella organisms were negative on October 8 and 9. The heterophile antibody reaction on October 9 was positive in a titer of 1:512. Urinalysis was negative.

The abdominal cramps persisted for 48 hours after admission and subsided with symptomatic treatment. On the 2nd hospital day, the temperature began to rise and the patient developed a low-grade fever that persisted for two weeks, the temperature ranging from 98.8 to 100°F. During that time he lost considerable strength and felt extremely tired. On the 8th day, enlargement of the left posterior cervical nodes was noted, and the swelling persisted throughout the hospital stay. The patient was discharged on the 18th day after having been afebrile for 3 days. The feeling of tiredness persisted for several weeks after discharge.

Diagnosis: infectious mononucleosis.

CASE 4. J. O., a 44-year-old sheet-metal worker, was admitted to a hospital on March 28, 1943, with chief complaints of fever and malaise. He had been fairly well until March 21, when there was onset of malaise and anorexia. He tempted self-medication with proprietary drugs and bed rest, but without relief. He then became aware of chills, sweats and afternoon sweats. Within the next few days began having severe occipital headaches. He consulted

his physician, who found that the temperature was 101°F. There was no cough or other symptoms of upper respiratory infection. The past history was not important except that the patient was employed as a sheet-metal worker in a manufacturing plant. Although he did not handle meat products, he often repaired metal runways used in the processing of meat products.

On admission, the temperature was 101°F., the pulse 110 and the respirations 20. Physical examination was negative. The red-cell count was 4,200,000, the hemoglobin 81 per cent, and the white-cell count 10,400, with 76 per cent neutrophils, 23 per cent lymphocytes and 1 per cent eosinophils. Urinalysis was negative. A blood Hinton test was negative. Agglutination tests on April 2 were reported as follows: typhoid and paratyphoid reactions, negative; undulant-fever reaction, positive in a titer of 1:405. X-ray examination of the chest on April 2 was negative.

The temperature remained elevated for 3 weeks after admission. During the 1st week it averaged 101°F. during the afternoon and evening and was considerably lower in the morning. During the 2nd and 3rd weeks the patient was afebrile in the morning, and the afternoon and evening temperatures varied from 99.6 to 102°F. There was no change in the physical findings. Recovery was uneventful following subsidence of the fever.

Diagnosis: undulant fever.

CASE 5. R. L., a 5-year-old boy, was admitted to a hospital on April 3, 1935, with chief complaints of fever and malaise. He had been well until 8 days prior to admission, when he became listless and fretful. There was general malaise and anorexia. The family physician found that the rectal temperature was elevated, varying between 99 and 103°F. Since there was no improvement after 4 days, hospitalization was advised. The past history revealed the usual childhood diseases. For several months the patient had been drinking raw milk. Adjoining the property on which he lived, there was a large piggery, but no history of contact with pigs could be established.

On admission on January 25, the temperature was 105°F., the pulse 120, and the respirations 36. The patient appeared pale and listless and was quite ill. The significant findings in the physical examination were marked splenomegaly, hepatomegaly and engorgement of the superficial vessels of the abdomen. The red-cell count was 3,640,000 and the hemoglobin 78 per cent. The white-cell count gradually rose from 3400 on January 21 to 5500 on February 27, with differential counts as follows: on January 21, 46 per cent neutrophils, 46 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils; on January 27, 36 per cent neutrophils, 52 per cent lymphocytes, 10 per cent monocytes and 2 per cent basophils; on February 3, 44 per cent neutrophils, 51 per cent lymphocytes and 5 per cent monocytes. Urinalysis was essentially negative. A blood Hinton test was negative. Agglutination tests on January 23 were as follows: typhoid and typhus reactions, negative; undulant-fever reaction, positive in a dilution of 1:32,805 and partially positive in one of 1:98,415. On February 15 and February 20, blood cultures revealed *Br. suis*. On January 21, x-ray examination of the chest was negative.

The temperature remained extremely high during the first 2 weeks of the illness. On January 28, therapy with a brucella vaccine was instituted, and there was a marked rise in temperature following each dose. On February 7, there was some diminution in the size of the liver and spleen, although the patient still appeared quite ill. Late in February, except for the febrile response following the administration of vaccine, the temperature became normal. Later, when the vaccine was discontinued, the temperature remained normal. On March 12, there was a recurrence of fever, and this persisted until March 20. Thereafter, except for an occasional rise to 100°F. during the afternoon and evening, the patient remained afebrile. There was an uneventful recovery.

Diagnosis: undulant fever.

CASE 6. R. H., a 27-year-old veterinarian, consulted his physician in December, 1939, with complaints of weakness and swelling of the scrotum. For several days he had tired easily, and this was followed by a painful swelling of the scrotum. The physician found that the temperature was 102°F. There was no history of urethral discharge preceding the onset of the present illness.

was composed of private patients treated by of us (L. J.); the second comprised patients treated by members of the visiting staff and residents of the Massachusetts Memorial Hospitals; third included patients with contagious disease, ally scarlet fever. A fourth group of cases, in ch healing was effected by draining the post-aural wound, is included for comparison.

In the first group there were 12 cases, all of which were operated on in the manner previously described. The postoperative course was uneventful in all cases; the patients were asymptomatic and temperature remained normal. Complete healing of the postaural wound and drum occurred in an average of twelve days. Two patients had a postaural abscess, and 1 had zygomatic mastoiditis on admission; all these wounds healed by first intention. The shortest hospital stay was six days, a patient leaving with a dry middle ear and a completely healed postaural incision.

An illustrative case is that of a twenty-two-year-old girl who had acute suppurative otitis media two weeks before admission and developed a large swelling over the zygomatic region one week before surgery. Trismus was marked, and a temperature of 101°F. was present. Operation revealed large areas of destruction in the mastoid and a subperiosteal abscess over the zygomatic root. The usual operation was performed except that in addition a stab wound was made over the zygomatic root and this area was drained for twenty-four hours. The sutures were removed in five days. The wound healed by first intention, and the canal was dry in seven days. It may well be that the stab wound was superfluous.

In the second group there were 8 cases of acute mastoiditis, in all of which the wound was closed by primary suture. Since several members of the staff did the operations, several different techniques were used. In general, however, a complete simple mastoidectomy was done. The cavity was irrigated with saline solution and dried, and the mixture of sulfanilamide and sulfadiazine was used to fill the cavity. The wound was closed either in a single layer with black thread or in two separate layers with catgut and silk. In no case was the wound drained. In some cases a myringotomy was done to provide adequate drainage through the middle ear. The average postoperative stay was fourteen days, and the postaural wound was healed and the middle ear was dry in all cases. Two cases required revision, since the wound broke down and the ear continued to drain, and some infected cells were found and removed. The cavity was filled with powder and sewed tightly as before. Healing by first intention and a dry middle ear resulted.

In the third group there were 25 cases. It must be remembered that any surgical procedure attempted on patients with scarlet fever is usually followed by delayed healing, and indeed in some severe cases

of the disease the healing response is an entity scarcely related to that found in patients without scarlet fever. These patients were treated as were the two previous groups, and the operative work was done by several different operators. The sulfanilamide and sulfadiazine powder was used to fill the cavities, and the wound edges closed in one or two layers, depending on the operator. Skin clips were often used for closure. Myringotomy was done when additional drainage facility was in order. No serious complications referable to the mastoid occurred. One patient developed erysipelas around the wound, one had a cervical adenitis requiring drainage, one had a hematoma of the wound requiring aspiration, and another developed a superficial abscess in the line of incision that resolved with hot compresses. The average postoperative stay was twenty-eight days, which is about half as long as the average hospital stay in the pre-sulfonamide days (see below). The postaural wound was healed in an average of nineteen days. It broke down in 9 cases, 6 of which eventually required revision. At the second operation it was usually found that some cells had been overlooked at the first operation. After these were removed the wound was filled with powder and tightly sewed. All these patients made uneventful recoveries. Many of the patients with scarlet fever complicated by mastoiditis were acutely ill, with a high fever. In all cases the temperature returned to normal within one to three days and the patients showed marked clinical improvement.

The fourth group comprised 26 patients with contagious diseases, 24 of them with scarlet fever, who required mastoidectomies in 1939. The average postoperative stay was over fifty-two days, the longest stay being one hundred and eighty-seven days and the shortest ten days. The following complications presented themselves: hemorrhage from the postaural wound; cellulitis of tissues around the wound, extending to the orbit; hemolytic streptococcus meningitis; and a diphtheritic membrane in the postaural wound.

SUMMARY AND CONCLUSIONS

Primary closure of postaural mastoidectomy wounds in 44 cases is reported. This method of treatment has been made possible by the advent of the sulfonamide drugs, which when used locally reach high concentration and virtually sterilize the wound. More than half the cases were those of mastoiditis complicating scarlet fever. In these, it was possible to reduce the period of hospitalization from an average of fifty-two days to twenty-seven days. Patients without scarlet fever went home with dry ears, and the postaural wound healed in an average of fifteen days.

In all of 12 private cases the treatment was successful, the patients being discharged with dry ears and healed postaural wounds. Primary cures were

used in processing meat products. These patients had no direct contact with animals or animal products.

To demonstrate how readily infectious mononucleosis and undulant fever may be confused, a typical case of each disease is presented.

The following cases, each demonstrating an unusual feature of the respective disease, are also discussed: infectious mononucleosis with involvement of the central nervous system, infectious mononucleosis with gastrointestinal manifestations, undulant fever of the malignant variety and undulant fever complicated by epididymitis.

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PRIMARY SUTURE OF SIMPLE MASTOID WOUNDS

LEIGHTON F. JOHNSON, M.D.,* AND PHILIP S. SPENCE, JR., M.D.†

BOSTON

THE purpose of this report is to record our experience in 44 cases of acute mastoiditis in which the patients were treated by means of primary closure of the wound after filling the cavity with sulfonamide powder. It will be generally admitted that if such wounds can be closed tightly at the time of operation, the risk of postoperative mixed infections, a prolonged hospital stay and frequent, painful postoperative dressings can be eliminated. With the advent of chemotherapy and its proved efficacy in treating infections, otologists have eagerly sought the best methods of using the sulfonamides in acute surgical mastoiditis.

It seems hardly necessary to state that the two objectives of surgery in acute mastoiditis are to save life and to secure a dry middle ear and thereby restore normal hearing. There obviously can be no compromise with these two fundamental aims in any contemplated change in surgical technic.

The technical demands for primary suture are exacting. The mastoid exenteration must be complete. Great care should be taken to remove all infected cells. The perilyabyrinthian cells are removed until the horizontal semicircular canal is sharply defined. The zygomatic area is thoroughly

cleaned out, and in a number of cases the incision is brought into view. The mastoid cavity is irrigated with normal physiologic salt solution followed by thorough drying of the cavity. If bleeding persists, adrenalin packs may be used to establish complete hemostasis. The cavity is filled with sulfonamide powder. It appears to make little difference in the end result which sulfonamide drug is employed. In the early cases sulfadiazine was used, more recently a combination of sulfadiazine and sulfadiazine powder in the proportion of 3 to 1 has been employed. The local concentration is so great that the mastoid cavity is sterilized and prompt healing ensues. The wound is closed in two layers, with more powder between layers. Interrupted catgut sutures are employed for the subcutaneous tissues, and the Poole suture with black thread is used for the skin.

If the patient's condition remains satisfactory the dressing is not touched for three days. If gauze over the incision is dry, it is not disturbed. On the fifth day, the dressing is again done and stitches are removed. If the middle ear is dry and the postaural wound has healed, the patient may leave the hospital after the seventh day.

The series of 44 patients covered in this report, all of whom were operated on within the last year and a half years, consists of three groups. 1

*Professor of otolaryngology, Boston University School of Medicine, chief of Oto-Laryngological Service, Massachusetts Memorial Hospitals
†Resident in otolaryngology, Massachusetts Memorial Hospitals

ved. Nine lumbar punctures in the 7 days after entry sealed persistently elevated initial pressures. The fluidained yellowish and cloudy and contained 100 to 2000 s per cubic millimeter, of which 88 to 100 per cent were ymophonuclear leukocytes. Pandy reactions continued ngly positive. A hemolytic *Staphylococcus aureus* was own from the spinal fluid as well as from the blood until day before death, when no growth occurred. The sulfazine level did not exceed 7.6 mg. per 100 cc. in the blood 5.5 mg. in the spinal fluid. Despite clinical improvement peratures of 100 to 103°F. continued. On July 25, the tient lapsed into stupor, and then into coma. The respiras and pulse became irregular, and he expired on the lowing day, 24 days after the onset of the illness and 7 ys postoperatively.

Autopsy. The gross anatomic diagnoses were as follows: rombophlebitis of the left and right cavernous sinuses; it superior petrosal sinus and ophthalmic veins; bilateral bital abscesses; basilar purulent leptomeningitis; infarc-

Through the 4-cm. operative defect in the left fronto-temporal region an elevation of brain tissue protruded.

The left frontal and temporal lobes of the brain were noticeably wider than the corresponding lobes on the right. Over both cerebral hemispheres the gyri were flattened and the sulci narrowed. An intense sanguinopurulent exudate covered the entire basilar surface of the brain and was particularly profuse around the chiasm and orbital portion of the frontal lobes, where separation from the dura was exceedingly difficult. There was a cerebellar pressure cone. The lateral, third and fourth ventricles as well as the aqueduct were dilated to about twice their normal size.

Small, irregular, yellowish areas of softness, varying in size from a few millimeters to 2 cm., involved the middle frontal gyrus, precentral gyrus, superior parietal lobule and central white matter of the left hemisphere (Fig. 2). No lesions of this type were found in the right hemisphere.

The cerebral cortex was edematous and in some regions poorly demarcated. The tissue at the lower portion of the



FIGURE 1. *The Sella Turcica, Showing the Distended Cavernous Sinuses and the Softened, Infarcted Pituitary Gland in Situ.*

tion of the pituitary gland; small recent cerebral infarcts. involving the left frontal, parietal and parieto-occipital lobes; cerebellar pressure cone; internal hydrocephalus; and fibrinopurulent pleuritis with empyema (right).

The most significant extracranial finding was encountered in the chest. The right pleural cavity was obliterated in its posteroinferior aspect by thin, easily friable fibrinous adhesions. Separation of the right middle and lower lobes from the chest wall disclosed a thin layer of thick yellowish purulent exudate. The left pleural cavity had a few similar adhesions but neither fluid nor exudate. The portion of the right lung bound to the chest wall showed spotted hemorrhage and exudate. Otherwise the lungs were normal in every respect, and nowhere were they consolidated or infarcted. The larger arteries and veins were patent and free of thrombi.

Both cavernous sinuses were greatly distended by firm, grayish-yellow thrombi, the left more so than the right (Fig. 1). In the left superior petrosal sinus and in both ophthalmic veins similar thrombotic material was found. In both orbits abscesses 1.5 to 2.0 cm. in diameter were encountered in the course of the ophthalmic veins.

left precentral gyrus was softened and hemorrhagic. The large cerebral arteries and veins were patent. No evidence of thrombosis was detected in either of these. The dural sinuses, other than those mentioned, were also free of thrombi.

The cavernous sinuses, sella turcica, pituitary gland and surrounding bone were removed en bloc, fixed in 10 per cent formalin, decalcified and stained with hematoxylin and eosin. The brain was fixed in 10 per cent formalin. Sections were stained with cresyl violet and hematoxylin and eosin. Other organs were fixed in Zenker's fluid and stained with phloxine and methylene blue.

Over the pleura adherent to the thoracic wall on the right there was considerable fibrinopurulent exudate, with some hemorrhage and organization. The subpleural vessels were congested. The underlying lung showed edema and slight hemorrhage into the alveoli. No pneumonitis was present.

In the liver there were scattered foci of lymphocytes not associated with necrosis.

The cells of the granulocytic series in the bone marrow were moderately hyperplastic.

The cavernous sinuses were filled with large, partially organized septic thrombi, consisting of polymorphonuclear

effected in 6 of 8 cases treated by the hospital staff and in 19 of 25 cases of contagious disease.

Primary suture requires close attention to the exenteration of all mastoid cells and to complete hemostasis.

Patients who were studied in the early portion of these cases were kept in the hospital longer than absolutely necessary in order to observe the effects of primary suture. Those admitted later, generally speaking, were allowed to go home in fewer days. Doubtless, results can be improved with standardization of operative technic.

No serious complications were seen in primary closure, even in the cases in which the sinus or dura was exposed. The temperatures promptly returned to normal after every operation, and no intracranial complications were noted.

In some cases the postaural wound ruptured at a short distance, but unless it became necessary to do a complete revision all these wounds healed spontaneously in a shorter time than was required by the earlier method. Sutures were removed about the fifth postoperative day.

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CAVERNOUS-SINUS THROMBOPHLEBITIS*

Report of a Case with Multiple Cerebral Infarcts and Necrosis of the Pituitary Body

AVERY D. WEISMAN, M.D.†

BOSTON

ALTHOUGH cavernous-sinus thrombophlebitis is a fairly common clinical entity, its cerebral complications have received surprisingly scant attention. Even such comprehensive volumes as those of Turner and Reynolds¹ and Eagleton² fail to stress intracerebral complications. Courville³ mentions the rarity of brain changes in this disease and holds with most other authors that leptomeningitis is the most frequent secondary pathologic change. Standard monographs and the recent literature confirm the impression that intracerebral complications in cavernous-sinus thrombophlebitis, other than leptomeningitis, are exceedingly rare, and no recorded example of implication of the pituitary gland has been found.

The case reported here offered an opportunity to examine the histopathology of cavernous-sinus thrombophlebitis in detail. The extensive intracerebral complications that were found raised points of practical interest.

CASE REPORT

D. F., a 13-year-old boy, was admitted to the Neurological Service of the Boston City Hospital on July 19, 1942. Seventeen days previously he had acquired a furuncle on his nose. One day after its appearance the left eye became swollen and prominent; within a few hours he became extremely drowsy and entered a local hospital in a comatose state. There he presented a stiff neck and a continuous temperature of 104 to 105°F. The following day he developed a right hemiplegia and proptosis of the right eye. On the 8th hospital day he had a generalized convulsive seizure. Under

treatment with sulfonamides, the clinical state improved slightly, although the spinal fluid showed persistent evidence of meningitis. The patient remained comatose for 11 days. At the end of 2 weeks he was transferred to the Boston City Hospital.

Physical examination on admission revealed an acutely ill patient, with a temperature of 104°F., a pulse of 136, and a blood pressure of 110/70. He was deeply stuporous. He understood simple commands when aroused but was unable to speak. There was moderate proptosis and considerable chemosis bilaterally. The sense of smell and visual acuity could not be examined; a right homonymous hemianopsia was suspected from the response to rough tests at the time of entry, but could not be verified. Both fundi presented edema and hyperemia, with blurring of the nasal margins of the disks. There was no response to painful stimuli on the right side of the face. There was a flaccid right hemiplegia affecting the face, arm and leg. The activity of the tendon reflexes on the right side was increased, with an equivocal Babinski sign on that side. The patient was incontinent.

The red-cell count was 2,500,000, the hemoglobin 45 per cent, and the white-cell count 14,500. The hemoglobin rose gradually to 69 per cent 2 days before death, and a white-cell count of 17,000 to 27,000 was maintained throughout the course of the illness. The nonprotein nitrogen was 28 mg. per 100 cc., the carbon dioxide combining power 36 vol. per cent, and the chloride 95 milliequiv. per liter. The urine gave an alkaline reaction and showed a specific gravity of 1.011, no albumin and no sugar. A rare red cell and an occasional white cell were noted in the sediment.

At the time of entry the initial pressure of the cerebrospinal fluid was 250 mm. The cell count was 2900 leukocytes, of which 1450 were polymorphonuclear leukocytes and 750 were erythrocytes. The fluid was yellowish and cloudy and contained a gelatinous clot. The Pandy reaction was strongly positive, with the total protein 534 mg., the sugar 57 mg., and the chloride 639 mg. per 100 cc.

Shortly after admission a left-sided trephination was performed to rule out subdural abscess, and none was found. The patient was somewhat improved the day after operation and was able to answer questions and to co-operate in a more thorough examination. The presence of a right homonymous hemianopsia was confirmed. Sulfadiazine was administered orally. During succeeding days he was able to move his right thigh, and his speech greatly im-

*From the Department of Neurology, Harvard Medical School, and the Neurological Unit of the Boston City Hospital.

†Assistant in neurology, Harvard Medical School; resident in neurology, Boston City Hospital.

on and stupor—were due to the thrombophlebitis and septicemia. The proptosis, orbital edema, chemosis, facial swelling and papilledema were caused by venous obstruction and lymphedema as well as orbital abscesses and swelling of the brain. The signs of involvement of the ophthalmic



FIGURE 5. Section through One of the Softened Areas Depicted in Figure 2

Note the thrombosed artery between two partially infarcted gyri (cresyl violet).

division of the trigeminal nerve, which was manifested by frontal headache and blunting of sensation over the cornea and forehead, were probably the result of toxic damage and edema.

The unique features of this case that merit special consideration are the multiple foci of necrosis in the left cerebral hemisphere, as a result of which there occurred convulsions, aphasia, homonymous field defect and a right hemiplegia, and the necrosis of the pituitary gland.

Focal cerebral signs in cavernous-sinus thrombophlebitis may arise in several ways. There may be retrograde thrombosis of cerebral veins from a cavernous sinus, with venous infarction or septic cerebral embolism developing from an acute bacterial endocarditis or pulmonary infection, with arterial infarction. A rare complication is a subdural empyema with venous infarction of the cerebrum, as reported by Kubik and Adams,⁵ but their case (Case 6) was associated with a primary sinus infection.

At autopsy the pathogenesis of the foci of cerebral necrosis was not evident. There was no subdural empyema, nor were the cerebral veins thrombosed. The shape and distribution of the lesions and the finding of occluded arteries, on the other hand, left no doubt that these were arterial infarcts. Although the infarcts can be attributed to thrombosed arteries, the source of their occlusion cannot be definitely established. The absence of primary arterial disease and the abrupt onset of the cerebral symptoms suggest embolic occlusion. No endocarditis

or pulmonary-vein thrombosis, however, could be found, which excludes the common origins of such emboli. Another possibility is that the arteries became thrombosed as a result of the contiguous leptomenigitis, but it is difficult to see how this could have occurred without accompanying thrombosis of the thinner-walled veins. The unilaterality of the lesions, limited to the left cerebral hemisphere, led to a careful inspection of the internal carotid artery. Within the cavernous sinus the internal carotid arteries showed a focal arteritis. Polymorphonuclear leukocytes had invaded the coats of these arteries, and over such inflammatory foci there was marked intimal proliferation. These arterial lesions correspond to the experimental infectious angiitis of Winternitz and Le Compte,⁶ who by injecting *Staph. aureus* produced necrosis in the wall of a vein, with thrombosis and an acute arteritis with intimal hyperplasia in an adjacent artery. Although the internal carotid arteries were diseased, there was no evidence of thrombosis. Thus the origin of the emboli remains conjectural.

Necrosis of the pituitary gland due to infarction has not previously been described in cavernous-sinus thrombophlebitis. No symptoms of pituitary insufficiency were exhibited by the patient, but from what is known of pituitary necrosis in other diseases⁷ this would hardly have been expected in so short a time. About 75 per cent of this gland was infarcted. According to Sheehan,⁷ 50 per cent or more of the pituitary gland must be lost before clinical evidence

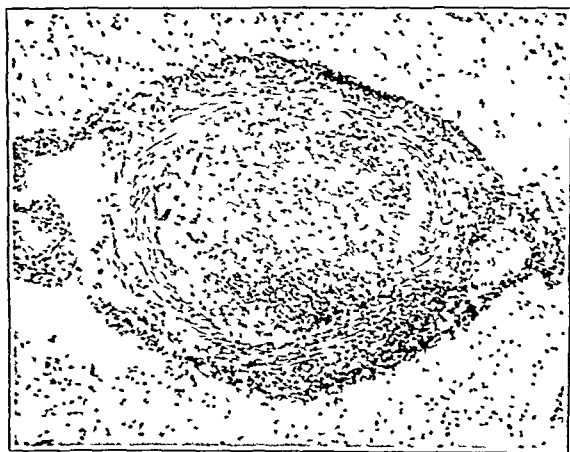


FIGURE 6 Section through a Thrombosed Artery
Note the periarterial inflammation, and the partial organization of the thrombus (cresyl violet)

of a deficiency appears. With the accurate methods of determining pituitary function that are now available, subclinical deficiencies occurring with destruction of a smaller amount of tissue can be determined. The increasing number of recoveries from cavernous-sinus thrombophlebitis with the use of sulfonamides and penicillin requires recog-

leukocytes, layers of fibrin, fibroblasts and hemosiderin-filled histiocytes (Fig. 3). The sinus walls were necrotic and invaded by polymorphonuclear leukocytes. Both carotid arteries were surrounded by the inflammatory exudate. In a few places polymorphonuclear leukocytes had penetrated the media and intima of the artery. Associated with such

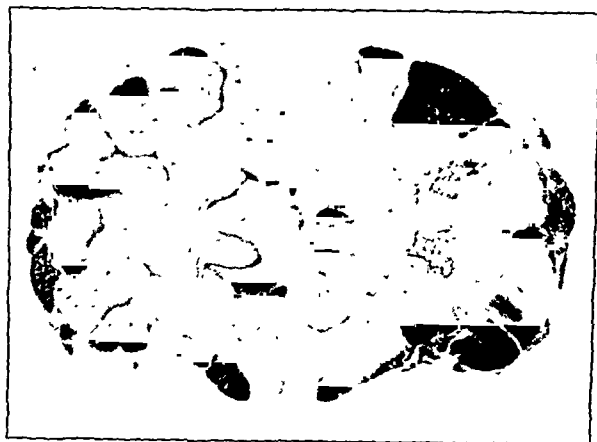


FIGURE 2. Section through the Frontal Lobes, Showing Several Irregular Areas of Softening in the Left Hemisphere.

local arterial infiltrations was a moderate degree of intimal hyperplasia and proliferation of subintimal fibroblasts. No fibrin, however, was deposited on the intima at such points, nor was there any other evidence of partial thrombosis of the artery. In the interstitial tissue between the sinus walls and the carotid arteries the inflammation was of a more chronic character, with an abundance of plasma cells and to a lesser extent histiocytes, some filled with hemosiderin. There was also an increase in fibroblasts.

Although the third, fourth, fifth and sixth cranial nerves were surrounded by suppuration, there was no evidence of

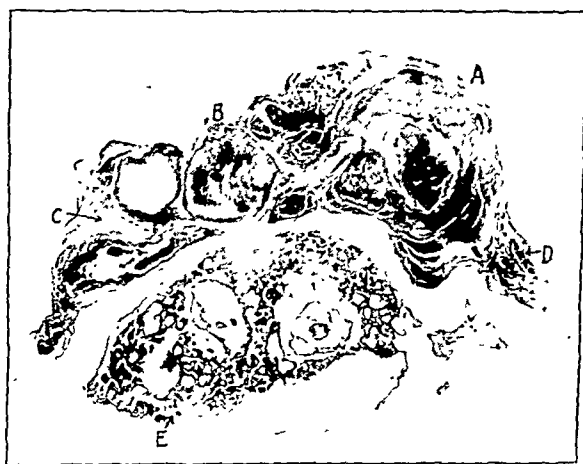


FIGURE 3. Coronal Section through the Cavernous Sinuses. Note the partially organized septic thrombi and the infarction of the pituitary gland. A represents the wall of the cavernous sinus; B, the thrombosed pituitary body; C, the internal carotid artery; D, the third, fourth, fifth and sixth cranial nerves in the wall of the cavernous sinus; and E, the sphenoid bone (hematoxylin and eosin).

direct inflammatory invasion. The myelin sheaths and axis cylinders were intact.

The pituitary gland showed an extensive central necrosis, evidently due to infarction (Fig. 4), and only a thin periphery of intact cells remained. A small number of polymorphonu-

clear leukocytes and red cells were found in the infarct tissue.

No acute osteomyelitis of the adjacent bone was found, nor was there any detectable abnormality of the meningeal membrane of the sphenoid sinus.

The leptomeninges over the cerebral convexities were somewhat thickened but showed no evidence of acute inflammation. Sections of the areas of softening in the cerebrum, previously described, disclosed complete destruction of nerve and glia cells (Fig. 5). Large numbers of histiocytes had infiltrated these areas. There was an increase in the size and number of capillary endothelial cells. Infiltration with polymorphonuclear leukocytes, either within the substance of the brain or around the small vessels, was lacking.

One small artery, cut longitudinally as it passed between two partially infarcted gyri, was completely thrombosed (Fig. 5). Its wall was surrounded but not invaded by lymphocytes and hemosiderin-filled histiocytes. A somewhat larger meningeal artery located near by and cut in cross section was thrombosed, and a fairly fresh collection of necrotic polymorphonuclear leukocytes and red cells filled its lumen (Fig. 6). At one point considerable fibroblastic activity, indicative of organization, was observed. Polymorphonuclear leukocytes and histiocytes both surrounded the artery and infiltrated its adventitia. Thrombosis of these arteries was



FIGURE 4. Section through the Infarcted Pituitary Gland Showing Central Necrosis and an Intact Periphery (hematoxylin and eosin).

unquestionably responsible for the adjacent infarction, but in many similar areas of infarction no thrombosed vessels were found.

Near one of the infarcts many small, discrete and confluent hemorrhages were encountered. These varied from mere local scatterings of red cells to large necrotic zones of hemorrhage. Even though many of the meningeal veins were congested, none appeared to be thrombosed.

DISCUSSION

The partly organized septic thrombi in the cavernous sinuses, the thrombosed ophthalmic veins and the orbital abscesses and edema of orbital tissue are characteristic pathologic changes in cavernous sinus thrombophlebitis and have been discussed in detail by Macewen,¹ Eagleton,² and Turner and Reynolds.³ There was an associated organizing purulent leptomeningitis that by obstruction of the foramen of Luschka was probably responsible for the internal hydrocephalus. The nasal furuncle was doubtless the source of the infection.

The pathological findings provide an explanation for the clinical picture. The general systemic symptoms — that is, malaise, chills and fever, prostra-

junctivas (see colored plate¹¹²), and resembles somewhat the ocular manifestations of argyria. The skin often shows varying degrees of generalized brownish to dull slate color as well as pigmentation of the hyperkeratotic papular lesions.

Mu, Frazier and Pillat,¹⁰⁸ using biopsy material, concluded that the skin and conjunctivas of patients with vitamin A deficiency contain both melanin-building ferments and melanin pigments as shown by the positive Dopa and silver reactions. They also noted that in the skin the melanin-building ferments and melanin pigment are reduced around

Tolmach and Graham¹¹³ report the case of a forty-year-old woman seen in New York who showed skin pigmentation due to vitamin A deficiency. They review the literature and emphasize the rarity of this finding in the white race in this country. Puscaru and Nitzulescu¹¹¹ think that the melanin pigmentation of vitamin A deficiency seen in persons of the darker racial groups should be considered as a manifestation of a special reaction, the intensity of which varies according to the particular capacity of the trophopigmentary tissue of different races, being most reduced in the white race. Pigmentation

TABLE 2. *Classification of Melanin Pigmentation of the Skin*
(From Becker and Obermayer,¹⁰² with Slight Modification.)

MELANOSIS NOT ASSOCIATED WITH AN INCREASED NUMBER OF MELANOBLASTS		MELANOSIS ASSOCIATED WITH INCREASED NUMBER OF MELANOBLASTS	
EXTERNAL CAUSES	INTERNAL CAUSES		
	Conditions Primarily of General Medical Interest		Conditions Primarily of Dermatologic Interest
Sunlight	Vitamin A deficiency*	<i>Erythrose peribuccale pigmentaire</i>	Ephelides (freckles)
Ultraviolet rays	Vitamin C deficiency*	Post-inflammatory condition	Pigmented nevus
Röntgen rays	Pellagra*	Chronic dermatitis	Neoplasms
Alpha rays from thorium-x	Sprue*	Dermatitis herpetiformis	Melanoma
Photosensitization to actinic rays	Anemias*	Urticaria with pigmentation	Melanotic epithelioma
Heat rays	Lymphomas*	Urticaria pigmentosa	Melanotic carcinoma
Mechanical irritation	Gaucher's disease*	Xeroderma pigmentosa	Mongolian spot
Chemical irritation	Niemann-Pick's disease*	War melanosis (Riehl)	Blue nevus
Vagabonds' disease	Acanthosis nigricans	Lentigo	Neurofibromatosis
	Scleroderma	Additional miscellaneous causes	Albright's syndrome*
	Ingestion of arsenic		Leschle's syndrome*
	Vagabonds' disease*†		Congenital neurocutaneous syndrome of melanosis of skin and central nervous system*
	Ochronosis*‡		Skin pigment spot localized over spina bifida occulta*
	Addison's disease		
	Acromegaly*		
	Cushing's disease*		
	Hypertthyroidism*		
	Pregnancy		
	Chloasma uterinum		
	Hemochromatosis (many cases)*		
	Additional miscellaneous causes*		

*Diseases added to original classification, on the basis either of data in the literature or of their similarity to disorders already classified

†Vagabonds' disease may have an internal as well as an external cause

‡Pigmentation chiefly in cartilage, skin pigmentation less constant

the hyperkeratotic follicle but increased in the near-by hyperplastic epidermis.

Pillat¹¹⁰ suggests that the main purpose of the conjunctival pigmentation is protection from the sun and daylight. Failure of the corneal epithelium to form pigment may be one of the reasons why the cornea sometimes undergoes marked changes (keratomalacia) in severe vitamin A deficiency. Argyria, arsenic ingestion, diminished liver function and the usual systemic disorders producing pigmented skin were all excluded as a cause for the pigmentation.^{109,110} Clinically, other deficiencies were not noticeable. That vitamin A deficiency was the cause of the conjunctival and skin pigmentation was suggested by its frequency in persons with xerosis, keratomalacia and follicular hyperkeratosis (70 to 80 per cent in one series) and its gradual subsidence when these other lesions healed from the administration of cod-liver oil.¹⁰⁹⁻¹¹⁰ Goldsmith¹⁰⁷ emphasizes the possible role of vitamin A deficiency in causing skin pigmentation.

of the skin and conjunctivas due to vitamin A deficiency is probably infrequent in this country because a deficiency severe and prolonged enough to cause xerosis and keratomalacia is but rarely seen.

Pigmentation and Vitamin C Metabolism

There is a considerable literature correlating or at least attempting to correlate skin pigmentation and vitamin C metabolism. Cornbleet¹¹⁴ and others¹¹⁵⁻¹¹⁷ give reviews of this subject. The vitamin C store in the adrenal glands diminishes in guinea pigs placed on a scorbutic diet. Melanin pigment in the skin has been shown to increase when vitamin C depots in the adrenal glands and the rest of the body are depleted and to diminish with administration of vitamin C.¹¹⁴ Pigmentation of the skin is frequent in scurvy and disappears with vitamin C treatment.^{114, 118} Hemosiderin and hematoïdin are formed in scurvy.¹¹⁸ The diffuse pigmentation sometimes seen, however, suggests overproduction of melanin as well as the presence of hemosiderin.¹¹⁸ The hyper-

tion of hypopituitarism as a possible consequence of this disease.

SUMMARY

A case of cavernous-sinus thrombophlebitis with extensive complications is reported. The complications included small cerebral infarctions, purulent leptomeningitis, bilateral orbital abscesses and infarction of the pituitary gland.

The clinical picture and pathology are discussed, with particular reference to the arterial basis of the cerebral infarcts.

Although several thrombosed arteries were found, no source could be ascertained. The possibility of hypopituitarism as a sequel of cavernous-sinus thrombophlebitis is suggested.

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MEDICAL PROGRESS

PIGMENTATION OF THE SKIN (Continued)*

HAROLD JEGHERS, M.D.†

BOSTON

MELANOSIS NOT ASSOCIATED WITH AN INCREASED NUMBER OF MELANOBLASTS

THE vast majority of melanin pigmentations encountered in medical practice fit into the group classified by Becker and Obermayer¹⁰² as melanosis not associated with an increased number of melanoblasts (Table 2). Melanin pigmentation results from the activity of melanoblasts normally present in the skin. Many of these follow or accompany drug or inflammatory reactions or various dermatoses and are of special interest to the dermatologist. In evaluating pigmentation one should therefore always inquire concerning a previous skin inflammation or lesions. Lentigo should not be confused with freckles. The former are dark-brown macules, usually 0.5 to 1.0 cm. in diameter, occur on the covered parts of the body as well as the face and hands and appear later in life than do freckles.¹⁰²⁻¹⁰⁴

External factors frequently cause melanin pigmentation. The best-known one is the common coat of tan from exposure to sunlight or to an artificial source of ultraviolet rays. Less frequently roentgen rays, radium rays, alpha rays from thorium-x and heat rays cause a significant degree of pigmentation. Mechanical and chemical irritations

are also important. External irritants play a role in causing the pigmentation of vagabonds' disease. Many agents applied locally, and some taken internally, may photosensitize the skin so that marked pigmentation occurs with only a limited exposure to sunlight.^{105, 106} The disfiguring pigmentation often brings these patients to the dermatologist.

Chloasma

Most pigmentations of interest to the physician result from internal causes. Chloasma is one of these and is defined as a yellowish to brown macular area, larger than common freckles, sharply demarcated and usually localized and increased by, but not dependent on, light.¹⁰⁷ If circumscribed on the face they are usually on the forehead or malar area. The term "liver spots" is sometimes used as synonymous with "chloasma," and because of their frequent association with menstrual and ovarian disorders or pregnancy the term "chloasma uterinum" is often applied to them. They may be associated with a variety of other conditions.^{102, 107} The mechanism of their formation is not clear.

Pigmentation from Vitamin A Deficiency

Adults in China, India and Japan with xerophthalmia and keratomalacia due to vitamin A deficiency have not uncommonly shown a striking pigmentation of the conjunctivas and skin.¹⁰⁸⁻¹¹² In the eye this pigmentation is of a peculiar brownish color, more marked in the lower fornix and bulbar conjunctivas than in the upper lid and bulbar

*From the Evans Memorial, Massachusetts Memorial Hospitals, the Fifth and Sixth (Boston University) Medical Services, Boston City Hospital, and the Department of Medicine, Boston University School of Medicine.

†Associate professor of medicine, Boston University School of Medicine, physician-in-chief, Fifth Medical Service, Boston City Hospital, and assistant physician, Clinical Staff, Evans Memorial, Massachusetts Memorial Hospitals.

the corium. No hemosiderin pigment was present in the skin.

It appears, then, that the pigmentation of sprue results from increased activity of the melanoblasts normally present in the skin. The responsible mechanism is not clear. Disease of the adrenal glands appears to be excluded. The chloride excretion in sprue is normal,¹³⁹ as is the histology of the adrenal glands.^{134, 135} Thaysen¹³⁵ has discussed the possible role of deficiency of vitamins B and C in producing pigmentation. Kaufman and Smith¹³⁸ believe that the role of avitaminosis in the production of pigmentary changes requires further investigation. It is of interest to note that pellagra is not uncommonly occurs in sprue patients.¹³⁴

The so-called "butterfly sign," an area of pigmentation of the face, narrow over the bridge of the nose and widening out over the cheeks, is frequently mentioned in the literature. At times it is accompanied by pigmentation of the mouth or tongue. It was for a time considered diagnostic of schistosomiasis, hookworm disease and infection of the urinary tract.¹⁴⁰⁻¹⁴² It was also considered in the earlier literature as a sign of intestinal tuberculosis.¹⁴² Sutton and Sutton¹⁴³ have commented on the supposed relation of mouth pigmentation to ancylostomiasis. It is difficult to evaluate the significance of these signs, but one could readily suspect a nutritional-deficiency mechanism.

Within the last few years 2 patients at the Boston City Hospital, a girl of fifteen and an adult woman, exhibited a curious syndrome of pigmentation of the skin associated with intestinal polyposis.¹⁴⁴ Both had had extensive gastrointestinal resections. Autopsy in each case revealed intestinal polyposis and normal adrenal glands. Pigmentation had been present in the girl before the intestinal operation. The pigment appeared to be melanin and was distributed in an acral fashion about the mouth, on the lips and over the hands and fingers as small dots and round patches. There is said to be a family in Boston several members of which exhibit this syndrome.

It is of interest that Hutchinson¹⁴⁵ in 1896 reported a case of cutaneous pigmentary syndrome in nine-year-old twins and identical with the pictures of our patients. Weber¹⁴⁶ later mentioned that one twin died at the age of twenty from intussusception. This circumstance suggests the possibility of these twins having had polyposis. The syndrome is not unknown in the literature. Metzger, Ohlmann and Half¹⁴⁷ report the case of a nineteen-year-old girl with polyposis and pigmentation of the skin. Polyposis is often familial. The possibility exists that the pigmentation represents an associated pigmentary anomaly rather than the result of a metabolic or nutritional disturbance of intestinal origin.

Pigmentation of the skin may occur in patients with gastrojejunal fistulas. I have seen such a

case, also one of tuberculosis of the ileum with skin pigmentation. Pigmentation of the skin may occur in celiac disease. It is well known that nutritional-deficiency states produce marked changes in the function of the small intestine, including absorptive defects.¹⁴⁸⁻¹⁵⁰

There is an extensive literature indicating that pellagra, which in itself is associated with skin pigmentation and other deficiencies, is frequently secondary to a wide variety of diseases of the stomach, small intestine and colon.¹⁵¹⁻¹⁵³ From clinical experience and perusal of the literature, however, one gains the impression that pigmentation of the skin without pellagrous dermatitis is, if not more frequent, certainly of a much more pronounced degree in diseases of the small intestine than in disorders of the colon.

Color of the Skin in the Anemias

All physicians are familiar with the pallor of the skin seen in patients with anemia. All other factors being equal, the degree of pallor is directly proportional to the loss of hemoglobin. Skin color in anemia patients, however, varies for other reasons than this. Wintrobe¹⁵⁴ gives an excellent account of these.

The lemon-yellow pallor of pernicious anemia can be attributed to the anemia together with mild bilirubinemia. It may also be attributed to the lack of biliverdin in pure hemolytic jaundice. Most patients with pernicious anemia now receive early and continued treatment, so that in contrast with the frequency in the pre-liver treatment era few patients remain untreated long enough to permit this sign of excess pigment metabolism to develop distinctively.¹⁵⁵ Minot¹⁵⁵ states that this characteristic appearance of pernicious anemia patients is about five times as rare as formerly. These patients may develop a brownish type of pigmentation that is either diffuse or blotchy.¹⁵⁶⁻¹⁵⁹ Vitiligo and premature graying of the hair are two other well-known pigmentary disturbances frequently seen.¹⁵⁶ The earlier literature contains many references that report cases of a melanin type of pigmentation of the oral mucosa^{146, 158, 160} (see colored plates^{160, 161}). In the experience of any one hematologist, however, this is a rare finding. The skin pigmentation appears clinically to be of the melanin type. Its pathogenesis is not clear. Formerly the arsenic therapy used was suspected,¹⁵⁹ but this theory is now untenable since patients not on arsenic therapy have shown this type of pigmentation.^{158, 160} The hemosiderin formed in this disorder may be a stimulus. Since absorptive difficulties have been demonstrated in the small bowel¹⁴⁸ the pigmentation mechanism may be similar to that seen in sprue. The role of the avitaminosis is not known. The pigmentation improves with treatment.

Similar pigmentation and vitiligo but probably of a milder degree are sometimes noted in hypo-

pigmentation of Addison's disease may diminish with vitamin C therapy.^{114, 116} It has been suggested that pigment and vitamin C in association with copper occur together in the skin, the pigment apparently serving as the anchor that holds vitamin C.¹¹⁴ Copper apparently hastens the darkening and precipitation of Dopa by ultraviolet rays, whereas vitamin C retards this precipitation.¹¹⁴ Several other writers have suggested that copper may play a role in causing skin pigmentation.^{119, 120} Comment is made on the possibility that disturbance of a copper, vitamin C and melanin balanced mechanism in the skin is the cause of the skin pigmentation in Addison's disease and scurvy.¹¹⁴ Vitamin C, tyrosine and Dopa absorb selectively the erythema-producing ultraviolet rays.¹¹⁴

The failure of some pigmentations to respond to vitamin C therapy has been ascribed to its oral use.^{117, 121, 122} Destruction of ingested vitamin C by infections in the upper bowel and failure of absorption because of achylia gastrica have been given as reasons.¹²² Parenteral administration has been recommended in such cases. Hoff,¹¹⁵ ascribes the skin pigmentation of gastric carcinoma, pernicious anemia, pancreatic disturbances and chronic gastrointestinal disturbances to such a mechanism. Counteraction of pigment formation by the administration of this vitamin is claimed. Chloasma has been reported to respond in a similar manner.^{114, 121, 122} Wilkinson and Ashford¹¹⁷ review the literature dealing with failure of vitamin C therapy in pigmentary disorders. Abt and Farmer¹¹⁶ mention favorable results with the use of vitamin C in treating pigmentation of the skin. The controversial nature of this field is thus apparent.

It has been suggested that photosensitivity on exposure to the sun with subsequent development of pigmentation may in certain cases be related to absence or diminution of certain vitamins, particularly vitamin A or C or both.¹²³

Further evidence of the influence of vitamin C on pigment metabolism is the recent demonstration of the need for this vitamin for the complete metabolism of tyrosine and phenylalanine. Pigmentation of this type appears to be conditioned not only by a vitamin C deficiency but also by the presence or absence of an excess of pigment precursors. Other information relative to vitamin C and pigmentation is discussed in the sections on Addison's disease and ochronosis.

Pigmentation of Pellagra

Pigmentation of the skin usually occurs in pellagra and appears to be of several varieties. The most frequent type is the deep tan or bronze color developing at the site of the pellagrous lesions as the acute phase of the dermatitis subsides.¹²⁴⁻¹²⁶ It is usually seen on the exposed portions¹²⁷—the face, neck and dorsum of the hands and lower legs (see illustrations^{125, 126} and colored plate¹²⁸). It may

develop in areas of the body exposed to irradiation but not to sunlight.^{125, 126} Stomatitis rather than pigmentation is the usual mucous-membrane manifestation.¹²⁴

A roughened, thickened (hyperkeratotic) pigmented area over pressure areas (the elbows, knees and so forth) (see illustrations^{125, 129, 130}) is considered one of the most characteristic skin lesions of pellagra, especially in mild chronic forms or as a sequel between flare-ups of acute pellagrous dermatitis.

Harris and Harris¹²⁵ in their monograph state, "At times there is a brownish pigmentation over the entire body, resembling and with much the same distribution as the characteristic epidermal discoloration seen in Addison's disease." Further simulation of Addison's disease is the occurrence of pellagra of hypotension, subnormal temperature, weakness and various gastrointestinal symptoms.¹²⁵ Many papers discuss the possible relation of the pigmentary syndrome of pellagra to adrenal function.^{125, 131, 132} Occasionally pathologic changes in the adrenal glands have been noted,¹³³ but in many cases with this suggestive clinical association no gross changes were seen in these glands.¹³¹ The occurrence of this type of diffuse pigmentary change in so many systemic diseases suggests strongly that other of the factors discussed in this review may be responsible.

Pigmentation of Sprue and Other Intestinal Disorders

Pigmentation of the skin is of common occurrence in sprue. It was noted by Thaysen in 12 of 34 cases in one series¹³⁴ and 7 of 10 cases in another,¹³⁵ in 22 of 32 patients by Snell^{136, 137} and in 4 of 6 patients by Kaufman and Smith.¹³⁸ The last workers have written an excellent account of all the cutaneous changes, including pigmentation, noted in the sprue syndrome.

The pigmentation is yellowish brown to brown, most characteristically occurring as sharply defined patches or spots, sometimes symmetrically disposed, on the forehead, nose and cheeks, about the lips and jaw and less frequently on the extremities or trunk. The pigmentation may also be diffuse and at times so extensive as to resemble the type seen in Addison's disease. It is exaggerated by exposure to sun, deepens with relapse of the disease and lightens or even disappears during remission or after treatment. The rarity of pigmentation of the mucous membrane of the mouth in sprue has been emphasized.¹³⁴

There has been considerable speculation concerning the nature of the skin pigmentation in sprue. Excessive hemolysis of red cells and jaundice from liver disease are readily excluded as the cause. Kaufman and Smith,¹³⁸ through special stains of biopsy material from a pigmented area, were able to demonstrate conclusively that there was an increase in melanin pigmentation of the basal cell and rete layers of the epidermis with no pigmentation

ed as bronze, tan, brownish yellow, subicteric brownish tan and bister (see colored plates^{183, 184}). pigmentation is not derived from bilirubin, jaundice is extremely rare.¹⁸³ It is further not to be due to the general deposition of siderin pigment or to Gaucher cells in the¹⁸³ Thannhauser¹⁸³ believes it to be due to melanin. Very rarely pigmentation of the mouth¹⁸³; in a reported case biopsy of the mucous membrane revealed the pigment to be melanin.¹⁸⁵ Gaucher cells do not involve the adrenal glands, tuberculous or scar tissue from siderosis of the organ may explain the occasional case with mucous-membrane pigmentation.¹⁸³ The reason for lesser degrees of pigmentation is not clearly understood. A malar flush of the cheeks may occur.¹⁸⁵

Of special diagnostic importance in Gaucher's disease is the wedge-shaped pinguicula-like thickening of the bulbar conjunctivas, brownish to ochre color, their bases abutting against the corneal margin and their apices extending symmetrically toward the inner and outer canthi (see colored plates^{183, 184}). They are readily overlooked unless the eyes are examined in strong daylight.¹⁸³ Thannhauser¹⁸³ states that although he has seen cases of the chronic adult form of Gaucher's disease in which skin pigmentation was present, he has never seen cases in which skin pigmentation was found and the brownish pinguicula-like thickening of the conjunctivas was lacking.

The other type of skin pigmentation has been emphasized by Bloem, Groen and Postma.¹⁸⁵ It occurs as a characteristic symmetrical pigmentation of the lower legs. The lower margin is rather sharply defined just below the level of the ankle, and the upper border is irregular, showing stripe-like projections with normal skin between them and reaching to variable distances below the knee, being most prominent on the anterior aspect of the lower legs¹⁸⁵ (see illustrations^{183, 185}). The color varies from yellowish brown to lead gray.¹⁸⁵ This pigmentation occurs in the absence of varicose veins, even in young adults. Biopsy of the pigmented area from one of the patients of Bloem, Groen and Postma revealed pigment giving a positive reaction for iron, localized in the dermis and some in small vessels and sweat glands, with the melanin content of the skin normal, findings suggestive of hemosiderin pigmentation.

The hemorrhagic diathesis in this disease and possible stasis of the blood in the leg veins from enlarged visceral organs (the liver and spleen) may be one explanation for this hemosiderin type of leg pigmentation. Deposition of the pigment in the corium may account for the lead-brown hue.

Splenectomy done in a patient with Gaucher's disease manifesting hemolytic anemia resulted in the disappearance of generalized pigmentation and the pinguiculas, but not of the pigmentation

of the legs, a point further suggesting that the two types of pigmentation are not the same.^{186, 187}

Skin pigmentation does not occur in the acute infantile form of Gaucher's disease, a point emphasized by Thannhauser¹⁸⁸ as differentiating it from Niemann-Pick's disease. The latter, which occurs only in infants, causes a gray-brown-yellowish diffuse pigmentation of the skin, especially on places exposed to the light (see colored plate¹⁸⁵).¹⁸⁹ The skin pigmentation of Niemann-Pick's disease is believed due to an increase of melanin. Thannhauser¹⁸⁸ believes that since the adrenal glands are infiltrated by Niemann-Pick's cells, the pigmentation syndrome may be similar to that found in Addison's disease.

Pigmentation of the skin is not a prominent feature of Hand-Schüller-Christian's disease or Tay-Sachs's disease.^{190, 191}

Acanthosis Nigricans

Acanthosis nigricans is a curious pigmentary disorder of the skin of considerable general medical interest because of its association with cancer in half the cases reported in the literature. The type not associated with cancer is called benign^{192, 193}; it occurs primarily in children, often appearing at puberty, progressing a variable degree and with an indefinite duration, and usually not causing or being associated with any serious systemic disorder. The skin in both these types has an identical clinical and histologic appearance. Disturbance of hormonal function of the sex glands has been suggested as a cause of the benign form. Other reasons for its occurrence have been given.¹⁹²

Curth,¹⁹³ in a thorough study and review of this subject, lists the extensive evidence correlating the association of acanthosis nigricans with cancer. This type of acanthosis occurs primarily in adults, especially those past middle age. Tabulations given in Curth's paper list its occurrence with various types of cancer as follows: breast, 9; lung, 4; stomach, 50; uterus, 8; liver, 12; pelvis, 4; abdomen, 8; rectum, 2; intestines, 2; ovary, 1, and so forth. These findings afford an excellent rationale for the dictum, "Acanthosis nigricans occurring in an adult is an indication for an exploratory abdominal operation." Curth believes that some property of the associated tumor may activate the skin lesions. Pressure on the intra-abdominal sympathetic nerves fails to explain many of the cases.

The pigmentary syndrome of acanthosis nigricans in its early stages is strikingly similar to that of Addison's disease, including the not infrequent involvement of the mucous membranes of the mouth.

Acanthosis nigricans causes additional skin or mucocutaneous changes, namely, exaggeration of the normal cutaneous markings, hyperkeratosis and verrucous and papillomatous changes (see

chromic microcytic anemia,^{162,163} but never the yellow pallor of pernicious anemia. The reason for the greenish or greenish-yellow color that led a former generation of clinicians to label hypochromic anemia in young girls as chlorosis (green sickness) is not well understood. Modern descriptions of chlorosis do not include the concept of a green pallor. A brownish hue of the skin in chlorosis is said to be much rarer than in the idiopathic hypochromic microcytic anemia of middle-aged women.¹⁶⁴

Pigmentation of the skin was frequently noted by Bomford and Rhoads^{165,166} in patients with refractory anemias. It varied from light to deep brown, was either spotty or diffuse and tended to be especially prominent on the exposed surfaces. In some cases a grayish or slate color was noted. Hemochromatosis was occasionally seen as a complication.^{165,167} These phenomena were especially noted in refractory anemia of the type with partly mature cellular marrow. Hemosiderin is thus to be strongly suspected as the cause of the pigmentation. It may stimulate melanin production directly in the skin or, more likely through deposition in the adrenal glands.

The studies of Whipple and Bradford¹⁶⁸ indicate that pigment abnormalities simulating hemochromatosis are of common occurrence in Mediterranean disease (erythroblastic type of anemia). Iron-staining pigment was noted in many organs but not in the skin. The adrenal glands were smaller than normal, with abundant iron-staining pigment in the glomerular zone. Grossly the skin looked pigmented. This pigmentation is difficult to evaluate since the disorder occurs in racial groups — Italians, Greeks, Syrians and Armenians — whose skin is normally of a dark complexion.

Ordinarily one associates the yellow color of jaundice with the hemolytic anemias, an association true in most cases. Not to be overlooked is the presence of hemoglobinemia and methemalbuminemia in certain of them. Fairley's^{169,170} classification of hemolytic anemias — hemoglobinuria, methemalbuminemia and hyperbilirubinemia; methemalbuminemia and hyperbilirubinemia; and hyperbilirubinemia alone — indicates the complexity of the problem of pigments in this group. The influence of these on skin color is not clear.

Pigmentation of the lower legs about and above the ankles probably of the local hemosiderin variety, appears to be not uncommon in congenital hemolytic jaundice^{171,172} (see illustrations^{171,172}) and sickle-cell anemia (see illustrations^{173,174}). Ulcers of the legs are frequent in these disorders. The pigmentation may occur about them or the healed scars, and occasionally without ulcer formation.

Pigmentation in the Lymphoma Group

Pigmentation of the skin aside from the discoloration caused by local skin lesions is one of the various dermatologic manifestations noted in

diseases of the lymphoma group.¹⁷⁵⁻¹⁸⁰ Jaundice may also be present with the lymphoma. Epstein and MacEachern¹⁷⁷ in a thorough study of 438 patients with diseases in this group, noted pigmentation of the skin in 15 (10 per cent) of 151 patients with Hodgkin's disease, in 2 of 122 with lymphosarcoma, in 2 of 90 with myeloid leukemia, in 1 of 60 with lymphatic leukemia and in none of 10 with acute leukemia or monocytic leukemia. Cole¹⁷⁹ noted diffuse pigmentation of the skin in 4 of 13 patients with Hodgkin's disease. Aside from the green color of local lesions, a diffuse olive tint of the skin may occur with chloroma.¹⁸⁰ A striking degree of melanin-type pigmentation in a patient presenting the clinical picture of a lymphoma would therefore be suggestive but not diagnostic, of Hodgkin's disease.

The skin pigmentation is brownish or bronze, often diffuse, with accentuation in the skin folds and may closely resemble that seen in Addison's disease. At times it is in the form of chloasma patches. The responsible factor is undoubtedly melanin. At times the skin manifestations resemble those of acanthosis nigricans.¹⁸¹ The hair may change color and become lighter.¹⁸⁰ Pigmentation of the mucous membranes of the mouth appears to be extremely rare in Hodgkin's disease.^{179,181,182} There are many reasons why pigmentation of the skin is frequent in Hodgkin's disease; arsenic therapy, generalized pruritus with scratching, x-ray treatment, irritation of the abdominal sympathetic nerves or pressure on the adrenal veins caused by enlarged nodes, malnutrition and avitaminosis are among the possible causes.^{178-180,182} Erythroderma due to a lymphoma may be accompanied or followed by skin pigmentation.¹⁸⁰ Direct involvement of the adrenal glands by a lesion of Hodgkin's disease is among the rare causes of Addison's disease.

Within recent years at Boston City Hospital there have been carefully studied 2 biopsy-diagnosed cases of Hodgkin's disease each with a degree of diffuse skin pigmentation resembling that seen in severe Addison's disease. There was no mouth pigmentation in either case. Skin biopsy showed only melanin pigmentation. Electrolyte studies of the blood sodium and chloride were normal. Erythroderma, local skin lesions, scratching, arsenic or x-ray therapy and involvement of the adrenal glands were excluded as causes of the pigmentation in these cases. Both patients were poorly nourished.

Pigmentation in Gaucher's Disease and Niemann-Pick's Disease

Pigmentation is frequent in adults with Gaucher's disease, and at least two distinct types have been described. One of these is localized in the exposed parts — the face, neck and hands. It may be diffuse or occur as chloasma patches vari-ously de-

tation. It has been my experience that medical students and interns have a hazy conception of this disorder. Textbooks on dermatology discuss it under pediculosis corporis. In a large municipal hospital one not infrequently encounters patients whose skin pigmentation is best explained on this basis. There is a considerable earlier and particularly foreign literature on the subject. The Germans refer to the disease as *Vagabondenkrankheit*.²¹⁸ Other synonyms are "vagabondism" and "vagabonds' discoloration." It has been defined as "a disease simulating morbus addisonii, particularly found in tramps and vagrants." From the literature^{102, 107, 218-223} and our own experience, the typical patient is a man in the older age group, unkempt in his personal habits, usually with pediculosis corporis and a history of infrequency of bathing or even changing the clothes and dietary deficiency, with or without alcoholism. Lesser degrees may occur in neglected elderly and female persons. The face—unless the patient is much outdoors—and the extremities show less pigmentation than does the body. The pigmentation is light to dark brown, and is accentuated about the waist and groins, between the thighs, in the axillas and over the back of the neck and upper back (see illustration²²⁴). The skin may show evidence of bites of pediculi and many linear scratch marks. Of interest is the frequent reference to pigmentation in the mouth,^{218, 219, 223} even in patients dying from other causes, with demonstration of normal adrenal glands at autopsy. Biopsy of the mucous membrane has been reported to show melanin,²²⁰ and this has been our experience in several such patients in whom normal electrodermal studies excluded Addison's disease. Bathing, local treatment of the skin lesions, clean clothes, good diet and multiple-vitamin therapy often cause the pigmentation to diminish in intensity. It is worth remembering that such cases may closely simulate the pigmentary features of the Addisonian syndrome. The skin pigment is melanin, with the melanoblasts in the basal epidermal layer Dopa-positive and the chromatophores in the corium Dopa-negative.²²⁰

Becker and Obermayer¹⁰² classify vagabonds' disease with the melanosis due to physical factors. Undoubtedly the lack of bathing, irritation from pediculi, scratching, unclean clothes, perspiration, toxic substances produced by pediculi and so forth are important. Nutritional deficiency is undoubtedly additive and may accent the melanin-producing ability of the above factors. Goldsmith¹⁰⁷ considers vitamin A deficiency important in vagabonds' disease, especially if the conjunctivas show melanosis. Deficiencies of vitamin C and the vitamins of the B complex may be equally significant, but relative data are not available. Of interest is György's²²⁵ observation that pediculosis is common in rats with chronic riboflavin deficiency but

is not observed in those deficient in other factors of the vitamin B₂ complex, and that riboflavin by mouth has a curative effect on this type of pediculosis in rats. Whether this concept holds for human beings is unknown. There appears to be no good explanation for the oral pigmentation noted in such patients.

Ochronosis

Patients with alkaptonuria cannot completely catabolize the tyrosine and phenylalanine of their food and tissue protein, so that an intermediate product, homogentisic acid, remains. Urine containing homogentisic acid is of normal color when voided but on standing turns brown or black.²²⁶ Fishberg's test²²⁷ enables alkaptonuria to be diagnosed immediately from a single drop of urine. Alkaptonuria is commonly considered an inborn error of metabolism present at birth. Over a period of years a pigment substance is deposited in cartilage,¹² the eye and to a lesser degree in the skin, causing, in later years of life, noticeable pigmentation and arthritis of the spine and large joints. Cardiac disturbances may also occur. Pomeranz, Friedman and Tunick²²⁸ have recently emphasized the roentgenologic features of this arthritis. The curious finding of calcification of the intervertebral cartilages and osteoporosis of the vertebral bodies enables the diagnosis of ochronosis to be made roentgenologically.

Exogenous ochronosis due to absorption of phenol used to dress wounds and ulcers, formerly frequent, has probably disappeared since the introduction of modern antiseptics.

Smith²²⁶ believes that Pick's explanation of the mode of production of the pigment in this disease is most plausible namely, "that, through the action of the oxidative ferment tyrosinase, the phenol substances in the exogenous group and the homogentisic acid molecule in the endogenous group are changed into melanin pigment, which is deposited in tissues." Virchow,²²⁹ in 1866, in studying histologic sections of darkly pigmented cartilage, noted that the pigment granules microscopically appeared pale yellow or ochre, hence the name "ochronosis" applied to deposition of pigment in the body tissue of patients with alkaptonuria.

Pigmentation of cartilage causes the ears and occasionally the nose or knuckles to appear blue, the predominant hue being, no doubt, the optical effect of pigment deep below the epidermis layer of the skin (see colored plates²³⁰⁻²³¹). The skin may become pigmented, especially as a butterfly-shaped brown pigmentation over the nose and cheeks or even more diffusely (see illustration²³⁵).^{230, 231, 236} Because the pigment granules are prominent in the deeper corium the skin pigmentation is apt to be a dark brown blue. Skin pigmentation is never so prominent a feature as is pigmentation of cartilage. At times the hands are pigmented.²³⁰

apy, with reappearance of the pigmentation crises due to rehydration.²⁵⁴ A melanin-pressing activity based on work with animals ascribed to the cortical hormone by Hamilton.²⁵⁵ There is a growing belief that the pigmentary changes are related in some way to vitamin C metabolism, as previously pointed out. Sodeman,²⁴⁹ Hoff,¹¹⁵ Wilkinson and Ashford¹¹⁷ and others give convincing but in part theoretical reasons for the validity of this belief. In vitro experiments show that vitamin C influences the Dopa reactions.^{114, 256} Several workers have reported that pigmentation in Addison's disease has improved with vitamin C therapy.^{116, 257, 258} Curiously enough, this idea appears to have attracted little attention. Rothman²⁵⁶ has recently produced convincing evidence that vitamin C metabolism influences skin pigmentation in Addison's disease. His work suggests that vitamin C may act to diminish hyperpigmentation due to a reducing action on preformed melanin rather than to prevent its formation. Rothman²⁵⁶ used serial colored photographs, silver and Dopa-stained skin biopsy material and the threshold of an erythema dose of ultraviolet light to study the influence of treatment on the pigmentation of Addison's disease. He confirmed the general impression that adequate control with cortical hormone and salt is without noticeable effect on skin pigmentation. He was then able to demonstrate, in the case of a thirty-seven-year-old woman, who was kept in good condition by continuous salt therapy, that the administration of 500 mg. of vitamin C daily by mouth for six months bleached the skin to such a degree that it could be readily recognized in colored photographs. Discontinuance of the vitamin resulted in steady darkening. The serum ascorbic level had been normal before the experiment was started.

Pigmentation in Pheochromocytoma

The malignant form of pheochromocytoma of the adrenal medulla commonly produces an entirely different clinical picture from the one characterized by attacks of paroxysmal hypertension, pallor, cold and clammy extremities, palpitation, headaches and other symptoms usually noted with the benign-tumor form of pheochromocytoma. Pigmentation is not listed as one of the features of the benign form.²⁵⁹ Weight loss, cachexia and skin pigmentation of the malignant form may produce a syndrome closely resembling Addison's disease.²⁶⁰

Pigmentation in Acromegaly

Although the influence of the hormone of the pars intermedia of the pituitary gland, and possibly a separate melanophore hormone affecting skin pigmentation, has been established for lower forms of animal life, this influence in human beings has not been established. Of interest is the recent

report by Fournier et al.²⁶¹ of successful treatment of vitiligo with a pituitary melanophore preparation both for local treatment of vitiliginous areas and for parenteral injection in regions remote from such areas.

Cushing,²⁶² in commenting on the pituitary control of dermal pigments, stated that pituitary disorders are likewise accompanied by appreciable pigmentary disturbances, although less conspicuously so than is Addison's disease. "The complexion of an acromegalic," he wrote, "as is well known, noticeably darkens in color, whereas the reverse is true of hypopituitary states in which the skin shows, in addition to its other distinctive peculiarities a characteristic pallor." Pigmentation of the skin in acromegaly is strikingly evident in many of the published photographs of such patients.^{263, 264} It is yellowish to brown and due to melanin; it occurs either as small frecklelike spots (see illustration²⁶⁴) or more diffusely, is prominent on the exposed surfaces but at times is noticeable on other parts of the body, and is said to be more frequent in women than in men. There are but few comments concerning involvement of the mucous membranes. Davidoff²⁶³ in a careful study of the clinical picture of acromegaly noted cutaneous pigmentation in 46 of 100 cases. Atkinson²⁶⁵ in reporting a more elaborate study of over 1600 cases remarks on the frequency of pigmentation but does not give the actual incidence. The mechanism of the pigmentation is not clear. Excess activity of a pigment-producing or pigment-controlling hormone of the pituitary gland is an explanation that, although attractive, requires further study for its final understanding and acceptance.

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The term "Cushing's syndrome" is applied to a striking clinical picture²⁶⁶⁻²⁶⁸ noted in association with cancer or adenoma of the adrenal cortex, basophil pituitary adenoma, probably with adrenal hyperplasia and adrenal hyperplasia alone, all such patients almost invariably showing in the pituitary gland the cellular changes noted by Crooke.²⁶⁸ The face is often flushed and reddish purple (see illustration²⁶⁶). Large purplish striae of the lower abdomen and upper thighs are frequent (see illustration²⁶⁶). Albright²⁶⁸ has emphasized the thin, reddish, possibly transparent skin. Extreme susceptibility to bruising and ecchymosis is frequent. All these color changes in the skin are easy to discern.

Cushing,^{266, 267} in his description of this syndrome mentioned pigmentation of the skin as a minor and not constant feature; he noted it in only 5 of 12 cases. Haymaker and Anderson²⁶⁹ in an extensive review of the literature of this disorder likewise assign pigmentation to the less consistently recorded features. Unfortunately, most papers give but little information about pigmentation other

Failure of the ears to show transillumination of light, due to pigment in cartilage, is diagnostic of ochronosis (see colored plate²³⁰). The cerumen of the ears and axillas may be pigmented.

Smith,^{226, 230} in 1942, published a detailed and stimulating account of the eye changes in ochronosis that probably occur in almost every case. He reports 4 cases and mentions others not reported, and stresses that ochronosis is far more frequent than is generally believed. The eye changes include pigmentation of the scleras, diagnostically distinct localized brown areas on the bulbar conjunctivas and pigment spots in the corneal limbus — best seen with slit-lamp observation. One of Smith's papers²³⁰ contains seven colored pictures of these eye changes. Patients with alkaptonuria should have a careful ophthalmologic study, including slit-lamp observation, for detection of early evidence of ochronosis.

Considerable interest has centered in the recent reports of alkaptonuria experimentally produced in guinea pigs by placing them on a diet deficient in vitamin C and feeding them 0.5 gm. of *l*-tyrosine daily.²³⁷ The addition of 5 mg. of ascorbic acid caused the homogentisic acid in the urine to disappear within one or two days and to reappear within one to three days after withdrawal of the ascorbic acid. Similar experimental results were obtained with two normal human subjects. Alkaptonuria has also been experimentally produced in rats from phenylalanine feeding.²³⁸ This work clearly indicates that the metabolic handling of tyrosine and phenylalanine is dependent on the presence in the body of an adequate amount of vitamin C. Using this information, Sealock, Galdson and Steele²³⁹ treated a sixty-five-year-old man suffering from alkaptonuria and ochronosis with large doses of vitamin C. Even doses of 4 gm. daily had no effect on the output of homogentisic acid. With large daily doses of vitamin C, however, the urine failed to turn dark even after standing several days. These writers suggest that their results do not preclude the possibility of a continued high intake of the vitamin in early life preventing the deposition of melanotic pigment in later years. This therapeutic suggestion would be well worth a trial if a patient with early ochronosis were encountered in clinical practice. The role of vitamin C in pigmentation appears a bit clearer from this work.

Pigmentation of Addison's Disease

Pigmentation of the skin is universally recognized as a constant and characteristic feature of Addison's disease. Its absence in chronic proved cases has been considered exceptional enough to merit a case report in the literature,^{240, 241} although it is generally agreed that in the rapidly developing type of disease pigmentation is occasionally of minimal degree or absent.

The pigmentary syndrome of Addison's disease has been more thoroughly and adequately studied than that of any other systemic disorder with cutaneous pigmentation.²⁴²⁻²⁴⁶ Chemical evidence²⁴⁷ and histologic evidence¹⁹⁵ show the pigment to be melanin. Other than increased melanin pigmentation, histologic sections are not characteristic. Pigmentation is most marked in regions normally pigmented or exposed to light or pressure. It appears particularly on the face, the neck, the back of the hands and particularly the knuckles (see illustrations^{248, 249, 250} and colored plates^{246, 248}). Pigmentation of the mucous membranes of the mouth and occasionally of the conjunctivas and vagina is an almost constant feature. Pigmentation of creases in the palms and soles and of the axillas and groins often develops. Pigmentation is diffuse, but pressure points and body folds may cause accentuation. The pigment color varies from grayish to brown. Minute black, frecklelike pigment may occur. The areolae, nipples and genitalia are often strikingly discolored. Vitiligo is not too rare (see illustration²⁴⁵).

Some papers discuss the possible mechanism of the pigmentation, whereas others simply state that it is not known. Sodeman²⁴⁹ in a recent review gives an excellent account of the literature.

The usual and older, but not proved, explanation states that it results from disease of the medulla rather than that of the cortex.²⁴² The mechanism suggested is that the diseased medulla, being unable to retain its normal store of epinephrine, releases it into the circulation, from which it or its oxidation product or precursor is deposited in the epidermal layer, eventually to form melanin. The similarity of epinephrine in chemical structure to its precursors tyrosine and dihydroxyphenylalanine has already been commented on. According to this hypothesis, Addison's disease in the acute form — chiefly cortical involvement — has but little pigmentation, whereas the chronic form, with both the medulla and the cortex destroyed, shows marked pigmentation. Against this theory are the pigment cases with an apparently good medulla but an atrophied cortex. Adrenalectomy in experimental animals does not usually cause pigmentation.²⁴² A recent report suggests that adrenalectomy may influence pigment metabolism if the vitamin C metabolism is changed at the same time.²⁵⁰ The influence of sulfur metabolism has been another cause discussed.²⁵¹

Most recent authorities state that control of the patient with modern hormone and salt therapy usually has no consistent or striking influence on the skin pigmentation.^{252, 253} Harrop et al. studied their cases with serial colored photographs of skin pigmentation. In fact, the occasional bleaching effect noted has been attributed to mechanical wearing away of the skin²⁵² and the edema of the skin likely to develop with the

apy, with reappearance of the pigmentation crises due to rehydration.²⁵⁴ A melanin-producing activity based on work with animals ascribed to the cortical hormone by Hamilton.²⁵⁵ There is a growing belief that the pigmentary changes are related in some way to vitamin C metabolism, as previously pointed out. Sodeman,²⁴⁹ ff,¹¹⁵ Wilkinson and Ashford¹¹⁷ and others give convincing but in part theoretical reasons for the validity of this belief. In vitro experiments show that vitamin C influences the Dopa reactions.^{114, 256} Several workers have reported that pigmentation in Addison's disease has improved with vitamin C therapy.^{116, 257, 258} Curiously enough, this idea appears to have attracted little attention. Rothman²⁵⁶ has recently produced convincing evidence that vitamin C metabolism influences skin pigmentation in Addison's disease. His work suggests that vitamin C may act to diminish hyperpigmentation due to a reducing action on preformed melanin rather than to prevent its formation. Rothman²⁵⁶ used serial colored photographs, silver and Dopa-stained skin biopsy material and the threshold of an erythema dose of ultraviolet light to study the influence of treatment on the pigmentation of Addison's disease. He confirmed the general impression that adequate control with cortical hormone and salt is without noticeable effect on skin pigmentation. He was then able to demonstrate, in the case of a thirty-seven-year-old woman, who was kept in good condition by continuous salt therapy, that the administration of 500 mg. of vitamin C daily by mouth for six months bleached the skin to such a degree that it could be readily recognized in colored photographs. Discontinuance of the vitamin resulted in steady darkening. The serum ascorbic level had been normal before the experiment was started.

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than that it occurs. Frequent mention is, however, made to it in the many published case histories.

Pigmentation of the skin in Cushing's syndrome appears to be of two types, both of which may occur in the same patient. One is a melanin type, as evidenced by a darker skin in the upper part or exposed parts of the body or accentuation of pigmentation over pressure areas, in the body folds, axillas and groins, under the breasts and so forth. This type is neither frequently nor prominently discussed. Bruising is common in this disorder, which, along with the elevated red-cell count, may predispose to hemosiderosis of tissues with pigmentation. Whether such a mechanism or stimulation of melanin formation by a hormonal mechanism occurs is not clear. If Cushing's syndrome is dependent on hyperadrenocorticism, it would be paradoxical to ascribe its pigmentation to this type of adrenal dysfunction when the classic example of marked pigmentation, Addison's disease, is produced by a destructive adrenal lesion. It remains to be clearly stated whether a marked melanin pigmentation is directly related to the Cushing syndrome.

In contrast to this is the much more evident hemosiderin type of brownish to bronze pigmentation frequently noted over the lower legs, from the ankle to below the knee. It is strikingly evident in many of the published photographs of patients (see illustrations^{266, 267, 269}) and is specifically considered by Weber²⁷⁰ to be hemosiderin in type. The tendency for patients with the Cushing's syndrome to bruise easily and bleed into tissue, the thinness and fragility of the skin, the poor muscle tone of the lower leg muscles, which limits muscular activity as an aid to the return of venous blood from the legs, the pendulous abdomen and the elevated red-cell count all predispose to frequent gross or microscopic deposition of blood in the skin of the lower legs, with transformation to hemosiderin pigmentation, and probably to some stimulation of melanin formation.

Pigmentation in Simmonds's Disease

In contrast to the frequently observed pigmented skin of acromegaly and the plethoric and dark skin of Cushing's syndrome is the pale and sometimes yellow skin noted so frequently in Simmonds's disease, a disorder attributable to a destructive process of the anterior lobe of the pituitary gland. The adrenal glands in Simmonds's disease are usually less than normal in weight and show marked cortical atrophy but relatively little medullary change, a finding that led Sheehan²⁷¹ to remark, "In view of the condition of the suprarenals it is of interest that skin pigmentation of Addison's disease type is practically never seen." Escamilla and Lissner,²⁷² in a review of 101 pathologically proved cases in the literature, noted that skin pigmentation was seen in 24 per cent of them.

Williams²⁷³ and other endocrinologists stress the lack of skin pigmentation in patients with Simmonds's disease who manifest an Addison type of syndrome is one of the most reliable signs in differentiating it from true Addison's disease. They also emphasize that, even when skin pigmentation is present, it is of minimal degree and not likely to be confused with the classic pigmentation of Addison's disease. This was strikingly true in 3 cases seen by me.

Sheehan²⁷¹ emphasizes pallor of the skin in this disease, attributing it in part to indoor existence. He further comments on a possible endocrine origin contrasting the pallor of Simmonds's disease with the purplish plethoric facies of Cushing's syndrome. The yellow tint of the skin in Simmonds's disease, especially the type resembling myxedema, may well be due to the low metabolic rate. The existence of carotenemia was demonstrated in at least one case of this disease.⁵⁸

Hamilton²⁵⁵ noted that cortical hormone (desoxycorticosterone acetate) suppressed melanin formation by melanophores of explants of skin ectoderm from embryos of a species of fowl (New Hampshire Reds). He remarks, "This result may be of interest in view of the fact that clinically it is observed that Addison's disease is accompanied by a darkening of the skin as though the normal inhibitor of pigment formation had been removed with destruction of the adrenal cortex."

It is of interest that pigmentation of the skin is but rarely seen with anorexia nervosa, a disorder likely to be confused with some forms of Simmonds's disease. Offhand, one might expect to see pigmentation due to avitaminosis in this condition but curiously enough, signs of vitamin deficiency in anorexia nervosa are uncommon. In complete starvation specific vitamin deficiencies have not been noted, probably because the reduced energy requirements are satisfied by the utilization of body tissues that are in themselves complete foods.²⁷⁴ No doubt the low level of the metabolism in anorexia also diminishes the requirements for vitamins.^{274, 275}

Elaboration by the pituitary gland of a substance stimulating melanin production in the skin and inhibition of melanin production by the corticoid hormone, as just commented on, constitute a balanced control readily upset by disease in either organ.

Pigmentation in Other Pituitary Syndromes

Pallor of the skin is of common occurrence in hypopituitarism.²⁶² Cushing emphasized that persistent freckles on exposed areas of an otherwise pale skin are characteristic of most hypopituitary cases (see illustrations of facies of patient with chromophobe adenoma²⁶⁷). In Fröhlich's syndrome the skin feels soft and delicate and is sometimes peculiarly white, thin and transparent—the skin

and "alabaster skin".²⁷⁶ The face frequently presents a bright malar flush to form the so-called "roses-and-cream" variety of complexion. Pigmentary spots, walnut-stain colored, small and rounded, resembling freckles and ranging in size from pinhead to pea size, are not uncommon²⁷⁶ (see illustration²⁷⁶). Similar spots may be seen in the cutaneous dystrophias of the Laurence-Moon-Biedl type (see illustration²⁷⁶). Diffuse pigmentation is evidently extremely unusual but has been commented on as occurring in an atypical variant of the Laurence-Moon-Biedl syndrome.²⁷⁷ A similar frecklelike pigmentary syndrome is noted in pituitary dwarfism.²⁷⁸

Pigmentation in Hyperthyroidism

A survey of a dozen or more standard general medical works, as well as of monographs on thyroid disease, lead one to conclude that pigmentation of the skin is noted in 3 to 70 per cent of patients with hyperthyroidism. The pigmentation may be diffuse or chloasma in type, may be limited to exposed surfaces of the body or be widespread, and varies in intensity from being barely noticeable to being as dense as that seen in Addison's disease.^{279, 280} Hyperthyroidism of long standing is more likely to have the marked and diffuse type. The pigmentation is brownish and is due to melanin. Rarely it is present in the mucous membranes of the mouth. The marked accentuation of pigmentation of the eyelids occasionally noted in hyperthyroidism is called "Jellnick's sign."¹⁰⁰ The pigmentation often fades following adequate therapy.

Equally striking in some patients is the marked degree of vitiligo. In fact, the literature contains not infrequent references to the association of hyperthyroidism, vitiligo and alopecia areata.²⁸¹

The mechanism of the pigmentation is not clear. The similarity of the pigment precursor tyrosine, the thyroid hormone thyroxine (a phenyl ether of the amino acid tyrosine with four iodine atoms) and di-iodotyrosine is to be commented on. Melanogenesis is inhibited through the sympathetic pathways. Sympathetic stimulation is predominant in hyperthyroidism, so that this mechanism, if operative at all, can explain vitiligo but not the pigmentation. Diversion of tyrosine for thyroid use might explain vitiligo, but again not the more consistently present pigmentation. The complex inter-relation of the pituitary and adrenal glands in hyperthyroidism is well known. The influence of these two structures on pigmentations has already been discussed. The possibility of deficiency of vitamins, especially those of the vitamin B complex, because of the known influence of increased metabolism on its utilization,²⁸² may in some way be concerned with pigmentation in this disorder. The rarity of pigmentation of the melanin type in myxedema has been mentioned.

Pigmentation and the Gonads

"One of the outstanding characteristics of a human male castrate is the paleness of the skin," according to Edwards et al.¹² These writers, using the Hardy recording spectrophotometer, studied skin color in castrates and eunuchoid patients before and after treatment with androgenic hormones. Untreated castrates were shown to have more carotene, slightly less melanin but more melanoid and generally diminished hemoglobin pigment in their skin than did normal males. It is of interest that this combination of pigmentary findings is somewhat similar to the normal pattern for women.¹¹ Eunuchoids with secondary hypogonadism showed no carotene change from normal and a variable modification of other pigments. One eunuchoid showed findings similar to those of the castrate group.¹² Treatment of the castrates with androgens increased both the melanin and the melanoid, reduced the carotene and returned the hemoglobin quantity and distribution pattern to normal. It was concluded that androgens have a profound influence on the vascularity and pigmentation of the entire human skin.

Hamilton and Hubert.²⁸³ using castrate and eunuchoid men, showed that tanning of the human skin after exposure to ultraviolet rays is abetted by the presence and negated by the absence of effective levels of male hormone substance in the body tissues and fluids. Hamilton²⁸⁴ noted disappearance with androgen therapy and reappearance on its discontinuance of the pigmented color of the skin below the eyes noted in a castrate male adult. He likened the changes in color about the eye with those noticeable in some women during various parts of the menstrual cycle. With the use of explants of skin ectoderm from embryos of New Hampshire Red fowl, it has been shown that testosterone is far more potent in its action on melanophores than are any of the female hormones and expands both the red and the black ones.²⁸⁵

Hamblen and Cuyler¹⁴ reported that the average daily androgenic titers in the urine of true blonds were distinctly lower than those of marked brunets. Hamilton²⁸⁵ concludes that "both the tanning process and its dependence on hormones for photograph-like 'development' are somewhat similar in women to those described in men, capable of induction in women by male hormone substance and influenced by female as well as by male hormones." Many other examples of in vitro or in vivo experiments demonstrating the influence of sex hormones on pigment metabolism and pigmentation are on record.^{286, 287} Variations in skin pigmentation during the menstrual cycle are well known.^{107, 288, 289} It has been suggested that the influence of estrin on melanogenesis is concerned chiefly with the normal distribution of pigment. Rocca²⁹⁰ has reported success with the topical application of an ointment containing estradiol in a climacteric pa-

tient with chloasmalike areas of skin pigmentation. The explanation suggested was that "estrin causes the disappearance of the abnormal pigmentation through a local effect on the melanocytes when it is applied on the skin or when it acts on the pituitary gland if used in injections, thus inhibiting the melanophoric hormone." The skin of women with arrhenoblastoma, the masculinizing tumor of the ovary, is said to become darker.²⁹¹

Although the details are not completely established, it is apparent that both the amount and the ratio of the male and female sex hormones influence the degree and normal sexual differences of distribution of melanin pigmentation of the skin in human beings. Control of pigmentation by gonadal hormones must therefore be considered along with the influence of the pituitary and adrenal glands in evaluating pigmentary disturbances in endocrine disorders.

Pigmentation in Pregnancy

Pigmentation of the skin is practically universal during pregnancy.²⁹²⁻²⁹⁴ It usually starts about the face, where it is known as chloasma gravidarum and varies considerably in intensity. It appears oftener as brownish areas of chloasma than as a diffuse pigmentation. Brunets manifest it more than do blonds. It is greatly intensified by sunlight. Besides the face, increase in pigmentation is noticeable in the linea alba, on the breasts, in and about the nipples and about the vulvar and anal regions.²⁹³ Nishizaki²⁹⁴⁻²⁹⁷ studied skin pigmentation in pregnant women, using a tintometer to grade color changes. Studying Japanese women, he demonstrated that the pigmentation increased over the entire skin as well as in certain characteristic areas where it was especially noticeable. He correlated the degree of pigmentation with various factors constituting the process of labor and requisite for the normal completion of labor, and concluded that the degree of pigmentation indicates to some extent whether a woman is well adapted to the process of pregnancy. As is well known, the hyperpigmentation clears considerably after pregnancy, but varying degrees of permanent residua in certain areas — the nipples and areolas, the linea nigra and so forth — may remain and constitute presumptive clinical evidence of a past pregnancy.

A hormonal control of the pigmentation of pregnancy is generally acknowledged, but the mechanism has not been clearly shown. It is of interest that injections of estrin are said to intensify pigmentation in certain areas, that is, the areolas.²⁹⁰

Occasionally, development of pregnancy in women suffering from a disorder characterized by skin pigmentation accents the degree of pigmentation.^{298, 299} This is especially true of the pigmentation of neurofibromatosis.²⁹⁹

Pigmentation in Parathyroid Syndromes

Ectodermal disorders are present in chronic hypoparathyroidism. Although dryness, roughness, puffiness, thickening and scaling of the skin are often observed, it appears that pigmentation is rare but possible.³⁰⁰ Skin pigmentation does occur with hyperparathyroidism.

Miscellaneous Diseases with Melanosis

Many other diseases not adequately described in the literature may be associated with melanin pigmentation of the skin. Still's disease, rheumatoid arthritis, certain of the tropical diseases such as Kala-azar and schistosomiasis, senile chronic peritonitis, cachexia due to tuberculosis and malignancy, and cirrhosis of the liver are other examples. The association of skin pigmentation with polycystic disease of the kidneys has been repeatedly mentioned in the literature.^{301, 302} Ljapman and Friedberg³⁰³ discuss the influence of subacute bacterial endocarditis in causing skin pigmentation. It is not seen in the active stage of this disease, but may occur to a striking degree in the bacteria-free stage. They also comment on the café au lait pallor so characteristically seen in this disease. Pottenger³⁰⁴ describes a bronzing of the skin that he believes indicates a disturbance in fat metabolism. This color differs from sun tan. It clears with treatment utilizing the heat-labile factor found in lecithin-rich foods. Whether this disturbance is related to melanin metabolism is not known.

(To be concluded)

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Annual Meeting, May 22, 1944

THE annual meeting of the Council of the Massachusetts Medical Society was called to order at 7:00 p. m. in the Georgian Room of the Hotel Statler, Boston, on Monday, May 22, 1944, by the president, Dr. Roger I. Lee, Suffolk; 218 councilors were present (Appendix No. 1).

The Secretary presented the record of the stated meeting held February 2, 1944, as published in the *New England Journal of Medicine*, issue of March 9, 1944.

Dr. David Cheever, Suffolk, moved the approval of this record. This motion was seconded by Dr. Charles A. Worthen, Essex South, and it was so ordered by vote of the Council.

REPORTS OF COMMITTEES

Executive Committee—Dr. Michael A. Tighe, Middlesex North, secretary.

This report, which is as follows, was presented by the secretary:

The Executive Committee of the Council met on April 12, 1944. It reviewed the report of the Committee on Membership. It approved this report and the recommendation contained therein. The report will be presented to the Council later in this meeting.

The Executive Committee reviewed the report of the Committee on Cancer. It approved this report and the recommendation contained therein. The report will be offered later in this meeting.

The Executive Committee reviewed the report of the Committee on Public Relations and approved it. The report will be offered later in the meeting.

The Executive Committee reviewed the report of the Committee on Postwar Loan Fund and recommends that this matter be laid on the table until the Council meeting in February, 1945, so as to afford time for its discussion by the district societies and opportunity for the members of the Society as a whole to express themselves on it through a return postal-card survey. Action on this recommendation will be sought later in this meeting when the committee's report is formally before the Council.

Dr. Tighe moved the acceptance of the report. This motion was seconded by Dr. William M. Collins, Middlesex North, and it was so ordered by vote of the Council.

Committee on Publications—Dr. Richard M. Smith, Suffolk, chairman.

The chairman announced that the committee had no formal report to offer. He spoke of a joint conference that this committee had held with the Committee on Legislation in compliance with a directive of the Council given at its last meeting. He added that the Committee on Legislation would report on this conference later in the meeting.

Dr. Smith also said that the *Journal* had received a 25 per cent increase in its allotment of paper. He spoke of how helpful this was in meeting what had

become a pressing problem. This increase, he added, was in recognition of the fact that many copies go to the armed forces.

Dr. Lee said that this report was accepted as a report of progress.

Committee on Arrangements—Dr. Gordon M. Morrison, Middlesex South, chairman.

This report, which was offered by Dr. Morrison, is as follows:

The results of the committee's work cannot be properly appraised and reported on until after this current meeting is over. We can, however, report that during the past year we have held a number of meetings at which the program and other arrangements for this annual meeting have been worked out. The program that will be presented tomorrow and Wednesday covers a wide range of topics that we hope will be of interest to the general practitioner. We have tried to include timely subjects and to secure speakers who are widely known in their respective fields.

We wish to call attention at this time to the exhibits, both scientific and commercial, and to request that everyone pay a visit to them. About 40 per cent more booths have been sold this year than ever before, and all members should register at each booth some time during the meeting. It should be remembered that it is the money received from these exhibits that enables us to pay the expenses of more guest speakers and for larger meetings each year, and unless all members show an interest in the exhibits, we shall not continue to attract them.

From the financial point of view this meeting is sure to be successful. The income has already been greater than ever before, and we hope to turn over to the Society profits of at least \$4000.

In this connection, it is interesting to review the loss or gain of former committees on arrangements (Table 1).

TABLE 1. *Loss or Gain from Annual Meetings.*

YEAR	LOSS OR PROFIT	AMOUNT
1929	Loss	\$1099.36
1930	Loss	2209.29
1931	Loss	3189.20
1932	Loss	1250.66
1933	Loss	332.43
1934	Loss	898.57
1935	Loss	1784.03
1936	Loss	1157.45
Total loss		\$11,920.97
1937	Profit	119.33
1938	Loss	578.26
1939	Loss	84.35
1940	Profit	708.79
1941	Profit	1065.05
1942	Profit	3287.75
1943	Profit	1750.16
1944	Profit	4000.00
Total gain	(estimated)	\$10,268.47

From 1929 through 1936, the committees were a drain on the finances of the Society—one year the cost of the meeting was nearly \$3200—and for those eight years the total cost amounted to nearly \$12,000. For the eight years since 1937, there have been only two years when there was no profit, and for those years a total profit of \$10,268.47 has been turned over to the treasurer of the Society. This striking change in the financial results of these meetings corresponds with the date that our executive secretary, Mr. Boyd, took over their business management, and we believe that great credit is due him for what

he has accomplished. Moreover, we sincerely trust that next winter the Committee on Finance will recall these figures and see that he is properly recompensed.

To all of those who have aided this committee this year we offer our thanks.

Dr. Lee announced that this report was accepted as a report of progress.

Committee on Ethics and Discipline — Dr. Ralph R. Stratton, Middlesex East, chairman.

The report, which was offered by the chairman, is as follows:

During the past year the usual list of complaints of unethical action on the part of fellows, requests for advice concerning ethical procedure and so forth have been received. Most of these complaints were of minor importance and easily settled in committee.

Three complaints of unethical practice were of so serious a nature that they should be mentioned briefly.

First, a fellow was accused of vicious and deliberate violation of Section 4 of Article IV, Chapter III, of the *Principles of Medical Ethics of the American Medical Association*. Section 4 reads as follows:

When a physician does succeed another physician in the charge of a case, he should not make comments on or insinuations regarding the practice of the one who preceded him. Such comments or insinuations tend to lower the esteem of the patient for the medical profession and so react against the critic. Investigation satisfied the committee concerning his guilt, and his resignation from the Massachusetts Medical Society was requested and received. The episode was considered closed.

Second, a fellow was accused of violation of Section 3 of Chapter II, of the *Principles of Medical Ethics of the American Medical Association*. Section 3 reads as follows:

A physician is free to choose whom he will serve. He should, however, always respond to any request for his assistance in an emergency or whenever temperate public opinion expects the service. Once having undertaken a case, a physician should not abandon or neglect the patient because the disease is deemed incurable; nor should he withdraw from the case for any reason until a sufficient notice of a desire to be released has been given the patient or his friends to make it possible for them to secure another medical attendant.

This accusation was of a rather serious nature. Investigation and hearings showed the accusation to be justified. After a formal discussion, the fellow, although a member of the Society for a number of years, was judged to be totally ignorant of what constitutes ethical practice. He was verbally castigated by the members of the committee and was referred to the President for a severe admonition. This admonition was administered and so reported to the committee. The case was placed on file.

Third, three fellows were accused of deliberate violation of Section 7 of Article I, Chapter III, of the *Principles of Medical Ethics of the American Medical Association*. Section 7 reads as follows:

Physicians should expose without fear or favor, before the proper medical or legal tribunals, corrupt or dishonest conduct of members of the profession. All questions affecting the professional reputation or standing of a member or members of the medical profession should be considered only before proper medical tribunals in executive sessions or by special or duly appointed committees on ethical relations. Every physician should aid in safeguarding the profession against the admission to its ranks of those who are unfit or unqualified because deficient either in moral character or education.

This accusation was thoroughly investigated. A hearing was given to each of the accused. As a result, the committee unanimously judged each of them guilty of said violation and requested their resignations from the Society. Subsequently the resignation of each of the

fellows was received and referred to the Committee Membership for recommendation to the Executive Committee of the Council. When the Executive Committee shall have passed on these resignations, the incident shall be considered closed.

Dr. Stratton moved the acceptance of the report. This motion was seconded by Dr. William A. Chapin, Hampden, and it was so ordered by vote of the Council.

Committee on Medical Education — Dr. Robert Monroe, Norfolk, chairman.

No report.

Committee on Membership — Dr. Harlan F. Newton, Suffolk, chairman.

This report (Appendix No. 2) was offered by Dr. Newton, who suggested that, inasmuch as it had been received in advance of the meeting by the Councilors it not be read. It was the will of the Council that this report should not be read.

Dr. Newton referred to the *Journal of the American Medical Association* and particularly to the data on medical licensure in the United States and territories appearing in the issue of May 13, 1943. He summarized an editorial that appears in the same issue as follows:

Throughout the years, failures among foreign graduates were very high. Nearly 50 per cent of foreign graduates examined failed in 1943, these examinations being conducted in the United States, Hawaii, Alaska and Puerto Rico, as compared with a failure of only 1 per cent of graduates of approved medical schools.

Dr. Newton moved the acceptance of the report. This motion was seconded by Dr. John B. H. Norfolk, and it was so ordered by vote of the Council.

Dr. Newton then said that the Committee Membership, in this report, recommended that Chapter V, Section 2 (b) of the by-laws of the Massachusetts Medical Society remain unchanged.

He moved the adoption of this recommendation. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council.

Committee on Public Health — Dr. Francis P. Denison, Norfolk, chairman.

No response.

Committee on Medical Defense — Dr. Arthur Allen, Suffolk, chairman.

The report which was offered by Dr. Allen, is as follows:

We now have ten malpractice suits pending; of these three new cases have developed during the past year. It has not been possible to dispose of any case during the year.

The total bills for legal services for 1943 was \$439. The committee has no other expense.

Our attorneys are handling our affairs with satisfaction. Although our budget for the coming year has been reduced from \$2000 to \$1500, we believe that there is much likelihood that the total amount will be used.

Two members of the committee are in active military service, and the work is being carried on by the three remaining members.

Dr. Allen moved the acceptance of this report. His motion was seconded by Dr. Albert A. Hornor, Norfolk, and it was so ordered by vote of the Council.

Committee on Society Headquarters — Dr. William H. Robey, Suffolk, chairman.

This report, which is as follows, was offered by Dr. Robey:

The committee has held a few meetings since its last report, and some important improvements have been made in the rooms of the Massachusetts Medical Society. These changes have been made possible by the generosity of the trustees of the Boston Medical Library. They have consisted of a complete renovation of the space formerly occupied by the *Journal of Bone and Joint Surgery* and also of the room now occupied by the assistant to the Secretary. The latest change is the installation of a closet for the storage of certain journals and memoranda belonging to the Society. Considerable time was spent on this project, and the closet has been finally installed at the cost of \$180, which is a considerable reduction in the price of the space originally planned. It is also hoped that in time we shall install an office of information, renovate the lobby of the Library and place a suitable sign on the façade of the Library indicating the headquarters of the Society, but these last improvements will have to wait until materials are available.

Dr. Robey moved the acceptance of this report. This motion was seconded by Dr. Daniel B. Reardon, Norfolk South, and it was so ordered by vote of the Council.

Committee on Finance — Dr. Francis C. Hall, Suffolk, chairman.

No report.

Committee on Industrial Health — Dr. Dwight O'Hara, Middlesex South, chairman.

This report (Appendix No. 3) was offered by Dr. O'Hara. He said that this committee had continued to work in close co-operation with certain state agencies, the Associated Industries of Massachusetts, the New England Conference of Industrial Physicians, the American College of Surgeons, the Procurement and Assignment Service and the Council on Industrial Health of the American Medical Association. He added that two of the members of the committee had attended the annual meeting of the last organization, held in Chicago on February 14, 15 and 16, 1944.

He spoke of a register that the committee continued to maintain of those physicians who might be interested in practicing industrial medicine. He added that the supply of physicians was in excess of the demand.

He called attention to the committee's report of October 7, 1942, which stated that the committee was "most perplexed to know how to reach . . . those who are employed . . . in the small plants that are now rushing war production." He added that it was obviously impossible for the small plants to establish a real medical department, although three quarters of the workers are employed in such establishments. He said that a promising approach

toward solving this problem in Massachusetts had been made by certain community-health nursing associations which had offered special part-time service to the small plants in their respective areas.

He stated that a third industrial-health program, to be held in Springfield, had been prepared but that it had to be canceled because a suitable meeting place could not be secured and because of lack of evidence of local interest and support.

Dr. O'Hara said that, during the winter, the committee's attention was called to federal legislation calling for appropriations to state departments of labor to promote industrial health. He said that the committee had disapproved this legislation, having the support of the chairman of the Committee on Legislation of the Society.

He added that the present period of unprecedented industrial activity and the dependency of industry on the good health of the workers for a high production rate made the time ripe for establishing the principles of industrial medicine in plants where they had never been thought of before.

Dr. O'Hara moved the acceptance of the report. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council amid applause.

Massachusetts Committee on Procurement and Assignment — Dr. Reginald Fitz, Suffolk, chairman.

This report (Appendix No. 4) was offered by Dr. Fitz.

Dr. Fitz moved the acceptance of this report. This motion was seconded by Dr. George L. Schadt, Hampden, and it was so ordered by vote of the Council.

Dr. Fitz moved that the President be authorized to establish a Postwar Planning Committee of such size and composition as he deemed advisable. This motion was seconded by Dr. Carl Bearse, Norfolk, and it was so ordered by vote of the Council.

Dr. Fitz moved that the Committee on Procurement and Assignment be discharged. This motion was seconded by Dr. Charles F. Wilinsky, Suffolk.

The Secretary, when addressed by the President in connection with this motion, said that inasmuch as the Massachusetts Committee on Procurement and Assignment was not a committee of the Society but a part of the War Manpower Commission, a federal agency, it was not subject to discharge by the Council.

Dr. Lee said that he took great pleasure in reversing a previous opinion expressed by him on this subject and ruled that this committee might be discharged, so far as the Society was concerned. It was so ordered by vote of the Council. (Dr. Fitz was applauded as he left the platform.)

Committee on Legislation — Dr. Brainard F. Conley, Middlesex South, chairman.

The report, which is as follows, was presented by the chairman:

The Wagner-Murray-Dingell Bills remain the same as stated in our last report. This committee believes, however, that each member of the Society should be on the alert at all times for reappearance of activity on the part of those interested in promoting compulsory health insurance.

Members of the committee have spoken before approximately seventy medical, social and service organizations throughout the Commonwealth, educating the members of those organizations concerning just how the Wagner-Murray-Dingell Bills tend to endanger the American way of living.

Perhaps the most generous and valuable piece of work done in the matter of acquainting the general public with this proposed national legislation was that done by the alumni of Tufts College Medical School at their annual dinner in March. Invaluable services were rendered at that time through the instrumentality of a member of this committee, namely, Dr. William E. Browne, who arranged for Dr. Morris Fishbein, editor of the *Journal of the American Medical Association*, to address the meeting and also had the address broadcast over a radio hookup. This committee expresses its grateful appreciation both to the alumni of Tufts College Medical School and to Dr. Browne.

On February 2, 1944, the following motion was passed by the Council:

That the Committee on Legislation meet with the Committee on Publications to the end that methods of education in medical economics be contrived.

On April 29, the chairmen of these committees met and discussed this motion and decided to have a meeting of both committees on the afternoon preceding this meeting of the Council. Both committees met at 3:30 this afternoon, and a round-table discussion was conducted. It was decided to limit the discussion to medicine in New England.

It was stated and understood that the Committee on Publications, through Dr. Nye, had already invited contributions from all district secretaries and all chairmen of standing and special committees. It was voted that for six months the Committee on Legislation and the Committee on Public Relations should be urged to contribute such matter as is pertinent for publication in the *New England Journal of Medicine*. This should cover the Blue Cross, the Blue Shield, cancer clinics, federal aid, loans for home-coming medical officers and similar subjects.

Dr. Conley moved the acceptance of the report. This motion was seconded by Dr. John B. Hall, Norfolk, and it was so ordered by vote of the Council, amid applause.

Committee on Public Relations—Dr. Albert A. Hornor, Suffolk, secretary.

The report, which was offered by Dr. Hornor, is as follows:

(1) There was a progress report from the Committee Appointed to Look into the Possibility of Better Publicity for the Massachusetts Medical Society. After considerable discussion by the Committee on Public Relations it was finally moved by Dr. Pelletier and duly passed that the former committee be encouraged to seek knowledge of needs for better publicity and ways of obtaining better publicity.

(2) The major part of the evening was devoted to a discussion of the Emergency Maternal and Infant-Care Program, as administered by the Division of Child Hygiene of the Massachusetts Department of Public Health under the direction of the Children's Bureau of the United States Government.

President Lee had invited Dr. Getting, commissioner of health of the Commonwealth of Massachusetts, to meet with the Committee on Public Relations and discuss this question. Dr. Getting arrived at 8:00 o'clock and was most helpful in answering every question which was presented to him by members of the Committee on Public Relations. It was evident that Dr. Getting seeks the help of the Massachusetts Medical Society in the administration and modification of the program as needed to afford the best possible care for

the families of soldiers and at the same time have it the way that the members of the Massachusetts Medical Society think best.

(3) Dr. Fallon's report about the meeting between the organizations and representatives of the Massachusetts Medical Society, held under the auspices of the Farm Bureau Administration in Worcester City Hall on February 9, 1944, was read. There was good accord between the farm organizations and the medical profession as represented at that meeting. What the farmers want is group hospital and medical care coverage by the Massachusetts Medical Society, as a result of the meeting and previous conversations between the farmers and the Blue Cross and Blue Shield, it seems very likely that it will be obtained in the near future.

(4) A report of the Subcommittee on Tax-Supported Medical Care to the Committee on Public Relations was made as follows:

(a) The Technical Advisory Committee of the Department of Public Welfare met with Dr. Mandelstam, adviser to the department. It was agreed, subject to the approval of the Massachusetts Commissioner of Public Welfare, that physicians and surgeons should be compensated for services rendered in understaffed hospitals, persons eligible for state-supported medical care. It was also agreed, subject to the approval of the Massachusetts Commissioner of Public Welfare, that fees should be 25 per cent below the Blue Shield schedule, and on medical cases \$4 should be paid for the first visit in the hospital and \$2 for subsequent visits.

(b) At the last meeting of the Committee on Public Relations the matter of dissatisfaction with the *State Formulary* was referred to the subcommittee. The Council had previously adopted a resolution approving the *Formulary* in principle and urging physicians treating state supported cases to accept minor inconveniences as a public service in the interest of proper economy. The subcommittee has inquired into the workings of the *Formulary* and believes that the original action of the Council should be supported, that the inconveniences to the profession, the druggists and the patients have not been greater than could reasonably have been expected, and that the department has been entirely reasonable and flexible in making adjustments regarding complaints. The *Formulary* now being revised so as to include corrections based on experience.

This report was accepted by the Committee on Public Relations.

Dr. Pelletier reported that in Franklin County the district society had decided to charge full rates for attendance tax-supported patients. This action was approved by members of the Committee on Public Relations with a formal vote.

Dr. Hornor, in presenting the report, called the Council's attention to the fact that it was fully set forth in the sheets of advance information. He asked permission to submit it by title only. In this the Council acquiesced.

He moved that the report be received. This motion was seconded by Dr. Donald Munro, Suffolk, and it was so ordered by vote of the Council. Dr. Hornor said the report contained no recommendations.

Dr. Richard Dutton, Middlesex East, was recognized by the chair. He spoke as follows in connection with Item 4 (b) of the report, which concerns the *State Formulary*:

Because of expressed dissatisfactions, the Committee on Public Relations reviewed the recent vote of the Council regarding the resolution approving the so-called "*State Formulary*." This committee reaffirmed its previous position. The *Formulary* has been approved by the Committee on Public Relations, by the Executive Committee and by the Council itself. The Committee on Public

lations now asks reapproval of its position. With such overwhelming endorsement, it seems almost hopeless to urge further consideration by the Council but, to some at least, it seems as if such approval would carry with it the voluntary surrender of one of the most cherished rights of the medical profession.

The minor or major inconveniences of the *Formulary* to the medical profession, to the druggists and to the patients, mentioned by the committee, are only trivial matters. Whether or not the department has been reasonable and flexible, as they claim, is immaterial, and revisions and corrections of the *Formulary* will not affect the fundamental issue involved.

This issue is whether or not the Council deliberately tends to approve in principle the right of the State Department of Public Welfare, or any other department, to even the right of the Massachusetts Medical Society itself, to dictate to the individual physician what he shall prescribe and in what quantities.

Because a few physicians and druggists may have been scrupulous is no reason for the Society to endorse totalitarian tactics. There are plenty of proper channels through which to check these abuses.

If we are to continue to have old-age assistance, let's keep it a self-respecting insurance, for which we are all contributing; and let's remember that such patients are just as much entitled to the newer drugs advertised in the *New England Journal of Medicine* and elsewhere as are their next-door neighbors, perhaps in slightly better circumstances. Such statements as, "Reimbursement by the State Department will be limited to these items" and "Prices listed are maximal," which occur in the *Formulary*, are foreign to American medicine and to American independence.

But above all, let's not give away the right of the physician to prescribe for his patient according to his own best judgment.

I hope the Council will not approve the *Formulary* in principle.

Dr. Dutton moved that Item 4 (b), so far as it relates to the *Formulary*, be not approved by the Council. This motion was seconded by Dr. Brainard Conley, Middlesex South.

Dr. Bagnall said that he had a very profound respect and admiration for Dr. Dutton, but that he disagreed with him in his interpretation of the portent of this section. He pointed out that, at a previous meeting, the Council had approved the *Formulary* in principle. He added that Dr. Dutton's dissatisfaction had been brought into the Committee on Public Relations and that the matter was referred to the Subcommittee on Tax-Supported Medical Care. He said that this subcommittee, of which he was chairman, decided to stand by its original recommendation and to ask the Council to reaffirm its endorsement of the idea. He added that it had the approval of the Committee on Public Relations and of the Executive Committee.

Dr. Bagnall denied that there was in this item any invasion of the right of the physician to prescribe what he wanted to prescribe. He called attention to the fact that many hospitals indulge in the practice of having a *formulary* and that this does not mean that, under all conditions, the physicians practicing in those hospitals are obligated to follow it. He added that, by the same token, whenever the doctor wanted to prescribe a drug not contained in the *Formulary* and the use of the drug was reasonable and proper, the State Department of Public Welfare would interpose no objection.

Dr. Bagnall said that there was nothing fixed in the matter of the *Formulary* and that revisions will be made from time to time, depending on changes in price or demands by physicians. He added that this was emphasized in the October 27, 1943, issue of the *Bulletin of the Massachusetts Pharmaceutical Association*, and he quoted from this bulletin as follows:

The Department of Public Welfare has agreed that druggists should not be confined to these items mentioned in the *Formulary*, but may dispense all items called for by prescriptions issued by doctors. It is the purpose of the Department of Public Welfare to urge all doctors to conform, so far as may be possible, to those items in the *Formulary*. This formulary will be amended with prices changed to meet market conditions.

Dr. Bagnall said that the Massachusetts Department of Public Welfare had approved this bulletin before it went to press. Dr. Bagnall quoted from a letter received by him, as chairman of the committee, from the Department of Public Welfare, as follows:

On January 3d I gave you in essence the contents of a letter which is in the process of being drawn up, indicating to local boards that the department will reimburse for the initial purchase of goods not on the *Formulary*, or priced in excess of the *Formulary*, and that we intend to supply the local boards with enough information so that repetition of excess price or purchase of goods not on the *Formulary* will not occur. In the exceptional instances we expect the doctors will give adequate reason for the necessity of exceptions, and they will be made.

Dr. Conley asked for an annunciation of the principle involved. Dr. Bagnall said that we were being called on to approve the idea that the Department of Public Welfare was doing the proper thing in issuing a *formulary* for the guidance of those doctors who were practicing under its control or influence.

Dr. Conley said that to his mind the question involved here was whether or not the Council should approve of the Department of Public Welfare telling the doctor what he should or should not write for. He expressed the opinion that the Council should not so approve.

Dr. Bagnall, in denying that any such question was involved, said that the Department of Public Welfare had "not restricted the right of any physician to prescribe anything which you and I would think was all right for him to prescribe, regardless of whether or not it is on the *Formulary*." Dr. Schadt asked Dr. Bagnall why, under such circumstances, there was a need for a *formulary*. Dr. Bagnall reiterated the thought that the *Formulary* was a guide.

Dr. William A. R. Chapin, Hampden, said that the Department of Public Welfare can, and probably will, do this thing regardless of the action of the Council. He added that he was going to vote for the motion because he was a member of the Massachusetts Medical Society and was not particularly interested in the saving of money by the State Department of Public Welfare at the cost of the doctor's privilege and right to recommend to a patient

the use of any drug which he, the doctor, thought necessary and that he did not believe that it should be necessary for the doctor to seek the permission of the Department of Public Welfare before so doing.

The motion was lost on a vote by the Council.

Committee to Meet With the Medical Advisory Committee of the Industrial Accident Board — Dr. Daniel J. Ellison, Middlesex North, chairman.

This report (Appendix No. 5) was offered by Dr. Ellison.

He made many explanatory additions to the report. He emphasized the fact that henceforth the surgeon on duty in hospitals will be paid for all emergency work done by him on industrial accident cases and that an emergency as used in this connection does not necessarily end with the first treatment but may extend over many days. He spoke of the acceptance by the chairman of the Industrial Accident Board of the theory that the costs of the medical care of those injured in industry should be assessed to industry and not to the medical profession.

He spoke of circumstances under which injured workmen who are policyholders in the Blue Cross may acquire better accommodations than those allowed by the Industrial Accident Board. Such a policyholder of a semiprivate-room contract with the Blue Cross may, on his own election, occupy such semiprivate quarters and the Blue Cross will pay the difference between the sum allowed by the Industrial Accident Board and that charged by the hospital for this type of accommodation, when such a difference exists.

If the attending doctor, however, decides that the exigencies of a particular case require hospital accommodations of a type that cost more than that allowed ordinarily by the Industrial Accident Board, the Blue Cross will not piece out the difference in such costs. The Industrial Accident Board will consider every such case individually and decide in each whether or not the additional costs are warranted.

Dr. Ellison said that freedom of choice of physician is provided for by the law and that, in cases in which the patient knows no doctor, that principle may be maintained by supplying him with a list of the members of both the regular and courtesy staffs of the hospital in which he finds himself and another list selected by the insurance company from among the members of the regular hospital staff.

Dr. Ellison said that it had been agreed that the transfer of a patient from one hospital to another would in no way prejudice his rights.

Dr. Ellison moved the acceptance of the report. This motion was seconded by Dr. Munro, and it was so ordered by vote of the Council. (Dr. Ellison left the rostrum amid applause.)

Subcommittee on Postpayment Medical Care (Bank Plan) — Dr. Elmer S. Bagnall, Essex North, chairman.

Dr. Bagnall reported as follows:

I crave your leave to give you an informal report progress, because we had a meeting only this afternoon with Mr. McCarthy, of the National Shawmut Bank, who has sponsored this plan in Massachusetts for the Massachusetts Bankers Association.

Mr. McCarthy has been to New York to consult with the American Bankers Association, which has been very much interested in this plan — so much so, in fact that it is going to spend several thousand dollars in working this thing out in Massachusetts as a guinea-pig state.

They have some material, which Dr. Ellison and I looked over this afternoon, with which both of us were very much impressed. They want our endorsement of all of it before it goes through, but I will not take time to rehearse again the steps that have gone before in this bank plan.

I should like to say also that the American Bankers Association and the Massachusetts Bankers Association would like to include the hospitals in this plan, and they are going to contact the Massachusetts Hospital Association, so that there can be a reasonably effectual plan of postpayment medical care, supplementing prepayment medical and hospital care. The dentists will likewise be consulted. This will take care of those people who have not been foresighted enough to provide for their medical and hospital care in advance.

Dr. Bagnall moved the acceptance of this report as one of progress. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council.

Committee on Prepayment Medical-Care Costs Insurance — Dr. James C. McCann, Worcester, chairman.

No report.

Dr. Hornor moved the acceptance of the report of the Committee on Public Relations as a whole. This motion was seconded by Dr. Walter G. Phippen, Essex South, and it was so ordered by vote of the Council.

Committee on Cancer — Dr. Ernest L. Hunt, Worcester, chairman.

Dr. Hunt offered the report (Appendix No. 6) by title. In calling the attention of the Council to the fact that the advance sheets contained the report in its entirety, he spoke as follows:

The chairman of this committee would like to express his appreciation for the action of the Council at the last meeting on the question of fees in these clinics. He believes that the action of the Council was a great help in enabling the committee to get together with the State Department of Public Health and bring about a change in the rules and regulations, which has eliminated the cause of the complaint that was registered at the last meeting.

The report of the committee is found on page 8 of the preprint, and should be modified to this extent, that the one member who was absent from the committee at the time the report was adopted, has signified, in writing, his approval of the report, which makes it unanimous.

There is the formal report appearing on pages 8 and 9 of the advance sheets, and there is included a copy of the rules and regulations as revised, and made official by action of the Public Health Council as of April 11, 1944.

The essential point in the modification of the rules and regulations, which is a concession, I think, and a very happy one, is found on page 11 and is Plan C, which reads:

This plan is somewhat similar to Plan A. All patients seeking consultation service are examined at the clinic and receive advice irrespective of their financial

status, but the Commonwealth is only billed for "such persons as may be in whole or in part unable to support or care for themselves" and no fee is collected from any individual.

That is satisfactory to the committee, and the committee recommends that the report be accepted, and that the Council express its approval of the revised rules and regulations as here submitted.

Dr. Charles C. Lund, Suffolk, moved acceptance of the report. This motion was seconded by Dr. Walter H. Pulsifer, Plymouth, and it was so ordered by vote of the committee.

Dr. Lund moved the approval of the rules and regulations of the State Department of Public Health in the conduct of the state-aided cancer clinics, as revised by the Department on April 11, 1944. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council.

War Participation Committee — Dr. William B. Breed, Suffolk, chairman.

This report, which was presented by the co-chairman, Dr. Ralph R. Stratton, is as follows:

The work of the committee has been admirably covered by Doctor Breed, the chairman, in his reports to the Council on October 6, 1943, and February 2, 1944. At the close of the last report Doctor Breed said:

The War Participation Committee believes that definite steps should be taken throughout the Commonwealth to devise methods to meet possible emergency medical needs in the event of a serious epidemic and will proceed to instruct the district war participation committees along the lines that are finally decided on, be it through hospitals, through district headquarters or by means of a combined plan, flexible enough to fit the needs of differing local conditions.

Subsequent to the February meeting the committee has taken steps to bring this about. A dinner meeting was held on March 1, to which the presidents of the eighteen district societies and the chairmen of the district war participation committees were invited. The attendance, although not 100 per cent, was very gratifying to the committee.

After the opening remarks by the chairman anent the subject under discussion, a free discussion was indulged in by all the members present. A motion was passed that the chairman of the central committee write a letter to the chairmen of all district committees asking them to call this matter to the attention of their district societies at their annual meetings and to send reports to Doctor Breed by May 1. This instruction was carried out and a fair response was received from the district committees.

A thorough study was made of the stenotype report of the dinner meeting and of the letters received. This study has resulted in the following conclusions:

(1) That under ordinary conditions all portions of the Commonwealth are adequately protected by medical personnel.

(2) That a mild epidemic could be covered by the existing medical manpower without undue hardship either to the profession or to the public.

(3) That in a severe epidemic, in spite of a shortage of medical manpower and of trained nurses and the lack of adequate hospital conditions, most of the material needs of the people could be met by an appeal to:

(a) The American Red Cross, which, through its Disaster Committee, is in a position to give immediate aid with housing facilities, food, clothing and beds, and a satisfactory number of nurses' aides; and to

(b) The local defense boards which, by their setup, can augment the work of the Red Cross.

(4) That in a critical shortage of medical manpower in any locality due to a severe epidemic, an appeal could be made successfully to the Medical Division of the Massachusetts Commission of Public Safety.

A cordial working agreement to this effect has been reached between the War Participation Committee of the Massachusetts Medical Society, the American Red Cross and the Massachusetts Committee of Public Safety.

Dr. Stratton moved the acceptance of the report. This motion was seconded by Dr. Bearse, and it was so ordered by vote of the Council.

Dr. Stratton moved that the report be publicized. This motion was seconded by Dr. Frank W. Snow, Essex North, and it was so ordered by vote of the Council.

Rehabilitation Committee — Dr. William E. Browne, Suffolk, chairman.

This report, which was offered by Dr. Browne, is as follows:

Your committee met once since the last meeting of the Council was held in February.

At this meeting Dr. Wilinsky discussed some phases of the rehabilitation program in this state. Mr. Louis M. Tracey, representing Mr. Herbert A. Dallas, supervisor of the Rehabilitation Section under the Commissioner of Education, outlined a contemplated program that will be based to a considerable extent on regulations governing the plans and program of vocational rehabilitation issued by the Federal Security Administrator during the last of the year 1943.

Mr. Dallas indicated that, when plans are completed for operation of this program, the members of the Massachusetts Medical Society can be of great assistance. Until we hear further from Mr. Dallas, under whose immediate supervision this program will be put into effect, no action by the committee seems necessary.

Dr. Browne moved the acceptance of the report. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council.

Committee on Postwar Loan Fund — Dr. George L. Schadt, Hampden, chairman.

Dr. Schadt read the report (Appendix No. 7) in its entirety. He moved the acceptance of the report. This motion was seconded by Dr. Peirce H. Leavitt, Plymouth.

Dr. Ellison spoke of the young doctors who had gone into the armed service immediately on the completion of their internship. Many of these young men, he added, were eligible for membership in the Massachusetts Medical Society. He asked if some arrangement could not be made whereby these young men might participate in the benefits of the plan.

Dr. Schadt replied that such an arrangement might be worked out at future meetings of the committee.

The motion was adopted by vote of the Council.

Dr. Schadt moved the immediate adoption of the recommendations contained in the report and the placing of this plan in immediate operation. This motion was seconded by Dr. Leavitt.

Dr. Munro was recognized by the chair and spoke as follows:

It seems to me that there was considerable doubt in the Executive Committee of the Council whether or not there had been sufficient distribution of the data in this report among the various district societies. At the meet-

ing of the Executive Committee there were many representatives from various districts who thought that they themselves and their members were not sufficiently familiar with the implications of this report to accept the recommendations at this time, in other words, they believed that an opportunity should be given to spread the contents of this report among the individual members of the various district societies.

Dr. Munro moved as an amendment that the recommendations of the Executive Committee with regard to this report be adopted. This motion was seconded by Dr. Leroy E. Parkins, Suffolk.

The Secretary, at the request of Dr. Lee, read these latter recommendations as follows:

The Executive Committee recommends, with regard to the report of the Committee on Postwar Loan Fund, that this matter be laid on the table until the Council meeting in February, 1945, so as to afford time for its discussion by the district societies, and opportunity for the members of the Society as a whole to express themselves on it through a return postal-card survey.

Dr. Leavitt thought that action should not be postponed, as recommended by the Executive Committee. He added that the doctors whom it was expected this fund might help were already returning and that the proposals had already been publicized in the *Journal* so that all those who would have to vote on this matter ought to be thoroughly conversant with the subject.

Dr. Ellison asked how the provisions of the G. I. Bill of Rights might affect judgment in this matter.

Dr. Hyman Morrison, Norfolk, said that the Norfolk District Medical Society recommended the adoption of the recommendations contained in the report of the Committee on Postwar Loan Fund.

Dr. Hornor, while approving the recommendations contained in this report, expressed some apprehension concerning the effect that their adoption might have on the nonprofit status of the Society. Dr. Schadt replied that this phase of the subject had been investigated by him and that the Commission of Banks had informed him that our status would not be affected by it.

Dr. Guy L. Richardson, Essex North, spoke as follows:

It is the path of least resistance to pass this thing without the amendment, but in most instances it means doubling the dues. I should like to have each member of the Society in each district given the opportunity to acquiesce to this thing, as I believe practically all of them will. I do not believe that the delay until February will seriously inconvenience anyone. I am personally in favor of Dr. Munro's amendment, and I am certainly in favor of Dr. Schadt's committee's report, but I should like to see it go that way.

Dr. Chapin thought the Council should defeat the amendment and adopt Dr. Schadt's motion. He asked if it were not true that the members could be assessed to the extent provided in the report but that they did not have to pay it. Dr. Schadt replied that any assessment levied by the Society is an obligation that must be met by the individual if his membership in the Society is to continue.

Dr. Bearse said that if the Council approved amendment, it did not mean that it disapproved recommendations contained in the report. All meant was that certain additional steps should be taken to find out the viewpoint of the members at large. He expressed approval of the amendment.

Dr. Parkins spoke as follows:

I wish to take up the line of reasoning of Dr. Bearse. I am in favor of helping anybody who needs help, any who has participated in this war, but I do not think any of us can be accused of being unpatriotic or stingy, thinking this over.

From the treasurer of the Society I learned that we have \$165,000 lying idle in treasury at the present time. I want yet to have anybody answer what those funds are being held for. It seems to me reasonable that we pursue thought, What are we proposing to appropriate funds? We propose to help men. What for? To borrow money they will pay back. What for? To go into the treasury of the Massachusetts Medical Society—\$150,000, out of \$165,000, or a total of over \$300,000. What are we going to use that for? I should like to know what answer is.

I am very much in favor of postponing the final action until the February meeting, not with any idea of being stingy or unpatriotic. No one can accuse any of us of that because we are in favor of this amendment.

Dr. Munro said that he personally favored adoption of the recommendations contained in the report. He pointed out, however, that when the report was before the Executive Committee for review, it provoked a good deal of discussion as to whether or not the members at large would favor the recommendations. It was thought best to find out about that before proceeding.

Dr. J. Harper Blaisdell, Middlesex East, asked how many cases now exist that need the type of help provided for in the recommendations contained in the report. Dr. Schadt replied that he did not know.

Dr. Fitz spoke to the question asked by Dr. Ellison, which had not been answered and which concerned the young doctor now in service who is not a member of the Society. He asked if there was any way in which the young man might be included. Dr. Schadt replied that he would like to see this done and that he thought it could be worked out.

Dr. Lee put the amendment. It was so ordered by vote (show of hands) of the Council.

Dr. Leavitt moved that the Society appropriate \$20,000 out of the \$150,000 that had been talked about to be turned over to the committee for working basis until February, provided that, if at that time the assessment went through, the money would be returned. Dr. Leavitt expressed some apprehension whether or not this motion was in order. The motion was not seconded.

Military Postgraduate Committee—Dr. W. Richardson Ohler, Norfolk, chairman.

The report, which is as follows, was offered by Dr. Ohler:

In the report presented to this body at the midwinter meeting, it was stated that the object of this program has been officially declared to be an effort to present the best medical knowledge on the respective subjects from the point of view of civilian medical practice. Attention was also directed in our previous report to the fact that this work represents a co-operative effort of the various New England state medical societies, the American Medical Association, the American College of Physicians and the American College of Surgeons, on the one hand, and the United States Army, Navy and Coast Guard, on the other.

Since the meeting in February, the work of your committee has progressed with an ever-increasing degree of co-operation on the part of all the organizations involved and with what we believe to be an increasing sense of appreciation from the various Army, Navy and Coast Guard installations served by this program.

In February, it was reported that fifty-five exercises had been held in nineteen military installations scattered throughout New England. Since February, another installation has been added to the group, and seventy-six exercises have been presented. This makes a total for the year of one hundred and thirty one exercises in twenty military installations.

That this work has received the whole-hearted co-operation of the officers of the Army, the Navy and the Coast Guard is attested by recent letters, brief extracts from which I shall now read.

Such a program cannot fail to have its effect in improving the professional standards everywhere, but I wish to emphasize the vital importance of this program at the smaller stations where the staff is limited. At these somewhat isolated stations, particularly, the stimulus provided by your meetings has been especially appreciated both locally and by this headquarters. J. J. Reedy, Col., M.C., U.S.A.

I wish to take this occasion to express our appreciation for the work involved in this effort on the part of your committee and on the part of the eminent lecturers who have given of their time and substance. I think all will agree that it has been a great success and of special value to the small and isolated stations where medical contacts are difficult to obtain. R. H. Laning, Rear Admiral (MC), U.S.N.

We all feel that it has been a distinct contribution to the war effort, and I speak for the medical officers when I say that we have all felt that we have benefited greatly from such conferences. It is my hope that these programs will continue so long as the war continues. Charles J. McDevitt, Senior Surgeon, U.S.P.H.S.

The success of this work is due to the splendid co-operative effort of all concerned. It is my particular pleasure at this time to speak very highly of the unselfish attitude of all the instructors, many of whom have been forced to give up a good deal of time in order to reach some of the isolated stations. Without the enthusiastic response by this group of doctors, the work could not continue.

Finally, it has been requested by the chiefs of all the military organizations involved that programs continue throughout the summer months.

Dr. Ohler moved the acceptance of the report. This motion was seconded by Dr. Hall, and it was so ordered by vote of the Council.

Medical Advisory Committee to Regional OPA — Dr. Joseph Garland, Suffolk, chairman.

This report, which is as follows, was offered by Dr. Garland:

The records of this committee, which now cover ten months' work, indicate that 2382 applications for extra rations have been referred by the local boards to the Regional Office of the OPA. Of these 1658 have been granted in some part, and 727 have been denied. Members of the committee reviewed 963, or 41 per cent, of the cases.

During the year the district served was enlarged to include the entire state, and was then merged with the Regional Office, covering all of New England. Since Rhode Island has been the only other state with a medical advisory committee, the services of your committee have been utilized to aid in solving the rationing problems of the remainder of New England, which for the past month have numbered 131. The other state societies have been requested to appoint similar committees, and it is expected that this will be done at their annual meetings.

The recommendations of the Subcommittee on Medical Food Requirements of the National Research Council, published in October, were adopted by the national Office of Price Administration in March, and have been used as a basis for the decisions of your committee. The policy of the national office, however, as recently expressed, is to let the administration of the medical programs revert to the regional offices.

Frequent changes in point values have increased the task of trying to deal fairly with all applicants, and emphasize the necessity for a flexible program. The recent change to zero point values for all except certain choice cuts of meat has added particularly to the perplexities of the problem, since those who now request extra meat rations are obviously seeking luxury rather than medical-necessity diets. Many fantastic requests continue to be made, and more are referred to the Regional Office than formerly, as the local boards have been more limited in their scope of action.

The work of the committee has been greatly facilitated by the intelligent and efficient co-operation of Miss Elizabeth Golden, rationing aide to the Regional Office.

Dr. Garland moved the acceptance of the report. This motion was seconded by Dr. Maurice Fremont-Smith, Suffolk, and it was so ordered by vote of the Council.

In connection with this report, Dr. Lee said that comment in Washington had it that the work of the Massachusetts Medical Advisory Committee to the Regional Office of the OPA was far and away the best in the country.

Committee Appointed to Consult with Representatives of the New England State Medical Societies Regarding the Wagner-Murray-Dingell Bills — Dr. Walter G. Phippen, Essex South, chairman.

Dr. Phippen said that the committee had no report to offer and, inasmuch as the work of the committee had been finished, he moved its discharge. This motion was seconded by Dr. Hall, and it was so ordered by vote of the Council. (Dr. Phippen was applauded as he left the platform.)

Committee on Medical Information Bureau — Dr. Walter G. Phippen, Essex South, chairman.

Dr. Phippen reported as follows:

Your committee has considered the advisability of establishing a bureau of information at the Society's headquarters with considerable care. We have investigated and studied the bureaus that have been operating for many years in New York City and Philadelphia. Although the methods of operation of these bureaus differ in detail, their main object is the same, that is, to collect information from the various hospitals regarding operations, clinics, meetings and so forth, in one central place so that it may be readily available. Both these bureaus have been very successful and are evidently much appreciated by visiting physicians, as well as by local practitioners.

We were convinced of the need here in Massachusetts of such a bureau but before recommending it to the Council

thought that it would be helpful to try and get an opinion from the members of the Society. You have all received the prospectus, and many of you have returned the cards. The results of the poll have been quite illuminating. Up to the time of writing this report 908 replies have been received. Of these, 849 (about 95 per cent) have approved and 46 have disapproved; there were 13 blanks. Such a spontaneous reply speaks for itself. Some members wrote accompanying letters favoring the idea in more detail. One interesting card came from a doctor in Vermont who said that, although he was not a member of the Massachusetts Medical Society, he thought that such a bureau was very much needed and would be very helpful to visitors. Most of those who disapproved seemed to have a mistaken idea that it would benefit only those in the Metropolitan Area, whereas it is primarily for visitors from all over the Commonwealth, and to aid those returning from service with the armed forces to find easily the graduate instruction they will need.

This bureau will supply information concerning the daily activities of the Boston hospitals and of other hospitals in the immediate vicinity of Boston. This information will deal with each hospital's schedules of operations for the day, medical and surgical ward rounds, clinics, the location of such clinics and the names of those presiding over these various activities. From time to time the bureau will make available a bulletin that will list fixed medical meetings and conferences held in the Metropolitan Area. In brief, its ultimate aim will be to serve the profession as a clearing house for all sorts of medical information. It is proposed to disseminate this information, except that contained in the bulletin, by telephone. With this end in mind, the headquarters will be kept open such hours as will meet with the needs of the busy practitioner.

The committee makes the following recommendations:

- (1) That a Bureau of Information be established at the headquarters of the Massachusetts Medical Society, 8 Fenway, Boston.
- (2) That the committee authorized by the Council and appointed by the President to study the subject be authorized to supervise its installation.
- (3) That an appropriation not to exceed \$2500 be made for this purpose.

Dr. Phippen moved the acceptance of the report. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council.

Dr. Phippen moved the adoption of the recommendations contained in the report. This motion was seconded by Dr. Hall.

Dr. Parkins asked what the \$2500 would be used for. Dr. Phippen replied that it would be used for a separate telephone line, additional clerical service, stationery, postage and expenses incidental to getting out the bulletin.

Dr. Leavitt asked if this was going to be an annual appropriation. Dr. Phippen replied that this amount was only for the first year and that the committee did not know what it would cost annually until it had been tried out.

The recommendations were adopted by vote of the Council. (This action was greeted with applause.)

Committee to Meet with the Trustees of Middlesex University — Dr. Reginald Fitz, Suffolk, chairman.

This report was offered by Dr. Fitz. Subsequently, Dr. Fitz moved that the report of the committee, the discussion attending it and the vote of the Council concerning it be stricken from the record. This motion was seconded by Dr. Charles E. Mon-

gan, Middlesex South, and it was so ordered by vote of the Council.

Committee on Postgraduate Instruction — Dr. Reginald Fitz, Suffolk, chairman.

No report.

Committee on Physical Therapy — Dr. Arthur L. Watkins, Middlesex South, chairman.

No report.

Committee to Consider Expert Testimony — Dr. Frank R. Ober, Suffolk, chairman.

No report.

Committee on Automobile Insurance Claims — Dr. Henry C. Marble, Suffolk, chairman.

No report.

Committee to Study the Practice of Medicine by Unregistered Persons — Dr. Richard Dutton, Middlesex East, chairman.

No report.

Committee to Meet with the Massachusetts Hospital Association — Dr. Walter G. Phippen, Essex South, chairman.

No report.

Committee on Maternal Welfare — Dr. Judson A. Smith, Suffolk, chairman.

No report.

Committee on Ways and Means to Conserve Physicians' Energies — Dr. Elmer S. Bagnall, Essex North, chairman.

This report, which was offered by Dr. Bagnall, is as follows:

Inasmuch as the subsequent work initiated by the committee has been distributed between the Committee on Public Relations and the Committee on War Participation, we recommend that this be considered the final report and that the committee be discharged by the Council.

Dr. Bagnall moved the acceptance of the report and the discharge of the committee. This motion was seconded by Dr. Hall, and it was so ordered by vote of the Council.

ELECTION OF OFFICERS

Dr. Ralph R. Stratton, Middlesex East, chairman of the Committee on Nominations, reported as follows:

President: Dr. Elmer S. Bagnall, Essex North
Vice-president: Dr. Sumner H. Remick, Middlesex South
President-elect: Dr. Reginald Fitz, Suffolk
Secretary: Dr. Michael A. Tighe, Middlesex North
Treasurer: Dr. Eliot Hubbard, Jr., Middlesex South
Assistant treasurer: Dr. Norman A. Welch, Norfolk
Orator: Dr. Frank H. Lahey, Suffolk

The chair asked if there were any nomination from the floor. Dr. Ober moved that all nomination

closed. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council.

Dr. Stratton moved that the Secretary cast one ballot for the list of nominations as read. This motion was seconded by Dr. Paul J. Jakmauh, Norfolk, and it was so ordered by vote of the Council.

The Secretary announced that he had complied with his directive, and the President declared the officers elected. (Dr. Lee introduced each of the elected officers, except Dr. Lahey, who was not present, to the Council. They were greeted with applause.)

APPOINTMENT OF COMMITTEES

Dr. Elmer S. Bagnall, Essex North, president-elect, announced the committee nominations for 1944-1945. (The list will be published with the proceedings of the Society in a subsequent issue of the *Journal*.)

In making these appointments, Dr. Bagnall called to the attention of the chairmen of the various committees the provision in the by-laws that makes the president and president-elect members of all committees, and said that they should be notified of all meetings.

He added that there was a question whether or not some of these committees had finished their work. He pointed out that certain committees had not reported for a number of years and have no apparent activity. He said the by-laws require that each committee report in writing at least annually. He expressed the thought that the Society's slate might be cleared a little if some of these inactive committees could be taken care of by the Executive Committee.

Dr. Mongan, in arising for information, said that the President-Elect had appointed a committee to confer with the trustees of Middlesex University Medical School and that it was his understanding that the Council would have no such committee.

Dr. Lee pointed out that this committee had not been discharged. Dr. Mongan moved the discharge of the committee since there was no more work for it to do. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council. Dr. Bagnall announced that he withdrew the nominations to this committee.

Dr. Bagnall moved the approval of the nominations made by him. This motion was seconded by Dr. David D. Scannell, Norfolk, and it was so ordered by vote of the Council.

RESOLUTIONS

Dr. Lee read the following obituary of a deceased councilor:

Dr. John J. Cochran, of Natick, died May 1, 1944. He was in his forty-eighth year.

He received his degree from Harvard Medical School in 1923. He was a member of the courtesy staffs at the Newton and Framingham hospitals. He was an examiner for the local Selective Service board and a member of the American Legion and of the Harvard Club of Boston.

Dr. Cochran was also a member of the Council from the Middlesex South District.

His widow, two sons and two brothers survive.

The chair announced that, if there were no objection, the obituary would be spread on the records of the Council.

The chair called for resolutions on the death of Dr. Charles S. Butler, late treasurer of the Society. Dr. William H. Robey, chairman of the Resolutions Committee anent the death of Dr. Butler, said that these resolutions were to be read at the annual meeting of the Society, and that he would not, owing to the lateness of the hour, read them unless the President and Council so desired. The chair announced that, if there were no objection, the resolutions would be spread on the records of the Council without being read.

The resolutions are as follows:

Dr. Charles Shorey Butler was treasurer of the Massachusetts Medical Society from June, 1931, until the time of his death, which occurred on February 23, 1943.

Dr. Butler was born in Boston on July 6, 1870, the son of Charles Shorey Butler and Elizabeth Nancy Cummings. He graduated from Harvard College in 1893 and from the Harvard Medical School in 1897. After an internship at the Massachusetts General Hospital he entered private practice, served on the staff of one of the Boston hospitals and taught anatomy at Harvard. Quite early in his medical life he became interested in military medicine and served for seven years as assistant surgeon in the Massachusetts Volunteer Militia. At the time of his resignation he was a captain and assistant surgeon in the 8th Infantry Regiment. In 1915 he became a surgeon in the French Army, for which he was decorated by the French Government, having been made a chevalier of the Legion of Honor. On his return to this country he was commissioned captain in the Medical Reserve Corps of the United States Army and examined candidates for the Air Corps.

After several years Dr. Butler retired from active practice and teaching but continued to have a keen interest in the medical profession, in military medical work and particularly in strengthening preparedness among physicians in civilian life. He also retained his interest in the Medical Reserve Corps, in which he held the rank of lieutenant colonel.

Dr. Butler had an interest in finance and financial affairs; he liked to study the reports of corporations, and he became a trustee of several estates. As a result of his business interests he was selected for the office of treasurer of the Massachusetts Medical Society, and under his guidance the financial standing of the Society steadily improved. He bought and sold wisely, and his annual reports were received with applause.

Modest and self-effacing, his capabilities were sometimes hidden, but to those who knew him and worked with him, his courage and conscientiousness were ever apparent. He strove constantly to maintain the high ideals of the Massachusetts Medical Society, and his wise counsel will be greatly missed and long remembered by his colleagues.

NEW BUSINESS

Dr. Jacob Fine, Suffolk, was recognized. He said he had been inadvertently detained in getting to the meeting. He asked if it would be appropriate to make a few remarks concerning the report of the Committee on Membership. Dr. Schadt moved that Dr. Fine be given the privilege of the floor. This motion was seconded by Dr. Hall, and it was so ordered by vote of the Council.

Dr. Fine read a statement (Appendix No. 8) to the Council.

He moved the five-year exclusion provision adopted in 1942 as an amendment to the by-laws be submitted to the Council at its next meeting for further consideration, with a view to its revocation. This motion was seconded by Dr. Lund.

The question of a quorum was raised; 53 councilors were present. Dr. Lee announced a quorum present. The issue of a quorum again being raised and a quorum not being present, Dr. Fine withdrew his motion.

Following a motion by a councilor and a second by another councilor, the Council voted to adjourn at 11:15 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE OF COUNCILORS

BARNSTABLE

W. D. Kinney

BERKSHIRE

I. S. F. Dodd
C. F. Kernan
Solomon Schwager
P. J. Sullivan

BRISTOL NORTH

W. H. Allen
J. H. Brewster
R. M. Chambers
W. J. Morse, Jr.
J. L. Murphy
W. M. Stobbs

BRISTOL SOUTH

G. W. Blood
E. D. Gardner
C. C. Tripp
P. E. Truesdale
Henry Wardle

ESSEX NORTH

E. S. Bagnall
R. V. Baketel
N. F. DeCesare
E. H. Ganley
H. R. Kurth
P. J. Look
R. J. Neil
R. C. Norris
G. L. Richardson
F. W. Snow
C. F. Warren

ESSEX SOUTH

H. A. Boyle
C. L. Curtis
Loring Grimes
P. P. Johnson
A. E. Parkhurst
O. S. Pettingill
W. G. Phippen
E. D. Reynolds
H. D. Stebbins
P. E. Tivnan

J. W. Trask

C. F. Twomey
C. A. Worthen

FRANKLIN

H. L. Craft
H. M. Kemp
W. J. Pelletier

HAMPDEN

F. H. Allen
E. P. Bagge
W. A. R. Chapin
E. C. Dubois
G. L. Gabler
Frederic Hagler
G. D. Henderson
F. S. Hopkins
A. G. Rice
G. L. Schadt
J. A. Seaman
G. L. Steele

MIDDLESEX EAST

J. H. Blaisdell
R. M. Burgoyne
Richard Dutton
E. M. Halligan
M. J. Quinn
R. R. Stratton

MIDDLESEX NORTH

H. R. Coburn
W. M. Collins
D. J. Ellison
A. R. Gardner
W. F. Ryan
W. H. Sherman
M. A. Tighe

MIDDLESEX SOUTH

C. F. Atwood
E. W. Barron
W. B. Bartlett
J. M. Bary
J. D. Bennett
W. O. Blanchard
G. F. H. Bowers

Madelaine R. Brown

R. W. Buck
E. J. Butler
J. F. Casey
B. F. Conley
H. F. Day
J. G. Downing
C. W. Finnerty
H. Q. Gallupe
F. W. Gay
H. G. Giddings
H. W. Godfrey
J. L. Golden
A. D. Guthrie
Eliot Hubbard, Jr.
F. R. Jouett
A. A. Levi
A. N. Makechnie
J. C. Merriam
Dudley Merrill
C. E. Mongan
G. M. Morrison
J. P. Nelligan
Dwight O'Hara
Fabyan Packard
L. G. Paul
S. H. Remick
Max Ritvo
E. H. Robbins
M. J. Schlesinger
E. W. Small
H. P. Stevens
A. B. Toppan
J. E. Vance
Fresenius Van Nüys
B. M. Wein
B. S. Wood
Hovhannes Zovickian

NORFOLK

Carl Bearse
Arthur Berk
M. I. Berman
J. E. Burns
William Dameshek
G. L. Doherty
J. C. V. Fisher
Susannah Friedman
B. A. Godvin
J. B. Hall
H. B. Harris
R. J. Heffernan
P. J. Jakmauh
I. R. Jankelson
C. J. Kickham
C. I. E. Kickham
E. L. Kickham
H. M. Landesman
D. S. Luce
C. M. Lydon
D. L. Lynch
T. F. P. Lyons
F. P. McCarthy
H. L. McCarthy
F. J. Moran
Hyman Morrison
D. J. Mullane
G. W. Papen
H. C. Petterson
D. D. Scannell
Kathleyne S. Snow
I. W. Spellman
W. J. Walton
S. H. Weiner
N. A. Welch

NORFOLK SOUTH

C. S. Adams
D. L. Belding

F. W. Crawford
E. K. Jenkins
N. R. Pillsbury
D. B. Reardon
H. A. Robinson

PLYMOUTH

G. A. Buckley
P. B. Kelly
C. H. King
P. H. Leavitt
C. D. McCann
G. A. Moore
W. H. Pulsifer

SUFFOLK

A. W. Allen
W. J. Brickley
W. E. Browne
G. C. Caner
David Cheever
Pasquale Costanza
G. B. Fenwick
Reginald Fitz
Joseph Garland
R. L. Goodale
F. C. Hall
A. A. Hornor
H. A. Kelly
R. I. Lee
C. C. Lund
Donald Munro
H. F. Newton
R. N. Nye
F. R. Ober
F. W. O'Brien
J. P. O'Hare
L. E. Parkins
L. E. Phaneuf
Helen S. Pittman
W. H. Robey
H. F. Root
R. M. Smith
M. C. Sosman
E. F. Timmins
J. J. Todd
S. N. Vose
Conrad Wesselhoeft
C. F. Wilinsky

WORCESTER

C. R. Abbott
B. H. Alton
A. W. Atwood
George Ballantyne
E. J. Crane
J. J. Dumphy
J. M. Fallon
E. R. Leib
W. F. Lynch
J. C. McCann
A. E. O'Connell
H. L. Paine
R. S. Perkins
O. H. Stansfield
R. J. Ward
R. P. Watkins
B. C. Wheeler

WORCESTER NORTH

H. D. Bone
C. B. Gay
G. P. Keaveny
J. V. McHugh
F. A. Reynolds
B. P. Sweeney

PPENDIX NO. 2

REPORT OF THE COMMITTEE ON MEMBERSHIP (AND SUPERVISING CENSORS)

The following motion, offered by Dr. Jacob Fine, was passed by vote of the Council on February 2, 1944:

I move that the Committee on Membership be instructed to reinvestigate the merits of the five-year exclusion provision of the recent amendment with a view to reducing the time after a license is granted before membership in the Society is permissible.

This motion was preceded by a statement by Dr. Fine, which is hereby appended.

The Council may be interested in certain data regarding the foreign physicians licensed in Massachusetts. According to the *American Medical Directory* and the files of the Boston Committee on Medical

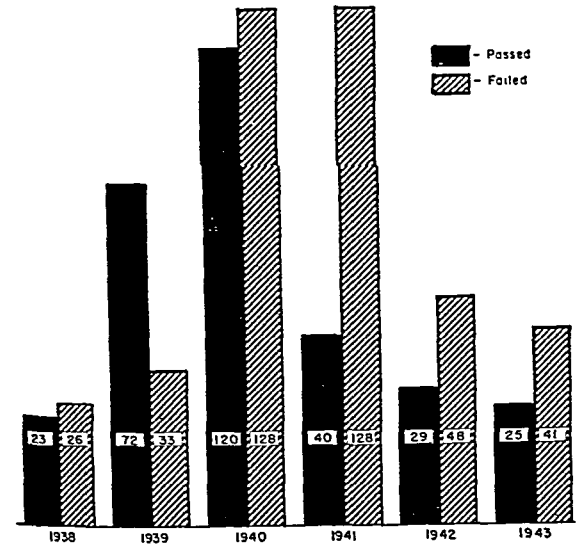


FIGURE 1. Results of Examinations by the Massachusetts Board of Registration in Medicine of Graduates of Foreign Medical Schools.

Emigres, a total of 165 foreign physicians have been licensed to practice in this state since 1934. The Committee on Medical Emigres has data in its files on all but 35 of the total number—that is, it knows the type of activity and the location of settlement of 130 of them. They are distributed as follows: 40 hold institutional positions exclusively, 66 practice a specialty or are in general practice in large or medium-sized cities, and 23 practice in small towns. They are settled in all parts of the State. Of the total number, 72 are members of the Society and 92 have not been admitted.

With these facts in mind, the following questions present themselves:

(1) Have any of the 72 foreign physicians who are members of the Society and who became members before the amendment to the by-laws was adopted acted unethically? Have any of them acted so as to prejudice the interests of the Society, their fellow practitioners or the profession at large?

(2) Of the 92 foreign physicians who are not members of the Society, all but 5 have been licensed for two or more years. Twenty-four hold institutional positions; 68 are in various specialties and general practice. Of this group of 68, have any acted during these two or more years in such a way as to prejudice the interests of their fellow practitioners or the profession at large?

The Committee on Medical Emigres has received complaints in three instances: in one case it could not get sufficient information; in a second, in which the physician was undesirably publicized in a newspaper shortly after his settlement, there was evidence that the physician was taken in by an overzealous young lady reporter apparently anxious to get material; and in the third case, now under investigation, the evidence is incomplete and conflicting, but the weight of evidence from the community itself is overwhelmingly in the physician's favor.

Rumors, vague accusations and generalizations regarding the demerits of these foreign physicians have been numerous, but specific demonstrable incidents of unacceptable practices have been exceedingly scarce and not out of proportion to what we experience among native-born physicians.

At the annual meeting in May, 1942, 44 per cent of those voting on the amendment to the by-law disapproved it. The Committee on Medical Education unanimously disapproved it. The machinery for excluding undesirable physicians from the Society existed before the amendment was adopted.

What experience did the Society or the profession have before or since the adoption of the amendment that justifies its continuance in its present form? The threat of inundation of the State by foreign physicians was never real, and today there is only a rare individual who might settle here, even if he were encouraged to do so.

It therefore seems appropriate for the Council to consider whether or not the amendment to the by-law is unnecessarily restrictive in its five-year exclusion provision.

At the beginning, Dr. Fine states that "according to the *American Medical Directory* and the files of the Boston Committee on Medical Emigres a total of 165 foreign physicians were licensed to practice in this state since 1934." When an applicant passes the examination of the Massachusetts Board of Registration in Medicine, he automatically becomes registered and licensed in this state. Information from the Board shows that in a six-year period (1938 to 1943, inclusive), 309 applicants who were graduates of foreign schools passed the examination of the Board, and 404 failed. This figure of 309 successful applicants between 1938 and 1943 is quite different from Dr. Fine's figure of 165 licensed men since 1934. This marked discrepancy of facts makes it difficult to evaluate the remainder of his statement.

I. For a true understanding of this problem, and particularly to see if the present by-law incorporating the five-year waiting rule for applicants of foreign schools was a departure from long-established custom in the Massachusetts Medical Society, it seems wise to review the history of the Society in relation to this by-law.

From studying the old by-laws it is apparent that the Society has attempted since its beginning to maintain high standards in the election of foreigners. It was in 1816 that the election of persons "educated without the Commonwealth" first arose. Such physicians might be eligible for membership if they had studied three full years under the direction of some reputable physician or surgeon or—as was said in 1832—if they had followed in their medical studies a course equivalent to that pursued by eligible candidates from Massachusetts.

This general policy was maintained for many years; in 1913, each candidate must have received a diploma from a medical school or college recognized by the Council and must also have passed the ordinary examinations, it being left entirely to the Committee on Medical Education and Medical

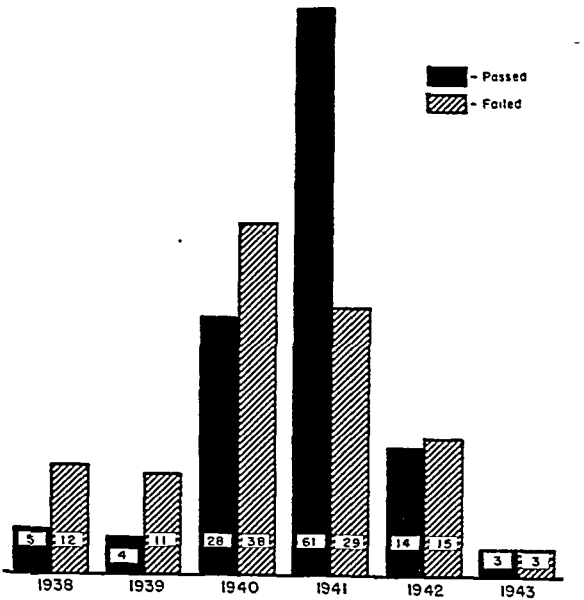


FIGURE 2. Results of Examinations by Censors of the Massachusetts Medical Society of Graduates of Foreign Medical Schools.

Diplomas to determine what foreign schools could be accepted as offering an education equivalent to that of our recognized domestic schools.

This procedure operated fairly well until an increasing number of foreign-trained physicians began to infiltrate Massachusetts. No one knew how good an education such people had received. I am informed by the chairman of the Committee on Medical Education that an evaluation of medical education in foreign schools, particularly that gained on the Continent, is almost impossible. Further, it is well known, particularly in Germany and Italy, that medical students may attend four or even five universities during

their medical course, taking their degree from the last attended university. Apparently the practice of a student transferring himself from different universities in order to study a particular science under a well-known leader in that field is not only generally practiced but also encouraged. Thus in 1939 the by-laws were rewritten to require that a graduate from a foreign medical school, to be eligible for membership, must have practiced for a minimum of five years and be recommended by a number of his colleagues who were fellows.

The expression "must have practiced for a minimum of five years" was evidently purposely loose: it might mean practice anywhere—indeed including internship as practice—or might be interpreted to mean a minimum of five actual years of practice within the confines of Massachusetts. This was done so that the Committee on Medical Education and Medical Diplomas might interpret the five-

III. There can be no question that there will be an additional foreign-educated physician on whom the five-year will work a hardship. The committee believes these cases rare. Outstanding physicians can be recommended by the Society for consideration for associate membership, thus become fellows of the Society in an honorary capacity without right to hold office or vote. Some physicians with American citizens have been educated in foreign medical schools. In a great many instances, if not in a large percentage of this group, inability to become a fellow of the Massachusetts Medical Society has not in the slightest hampered physicians from holding hospital appointments and continuing on an active practice in this state following licensure. It is well known that a great many of the best hospital staffs in this state admit substandard and foreign medical graduates to their courtesy staffs and allow them to treat their patients there, often without supervision of

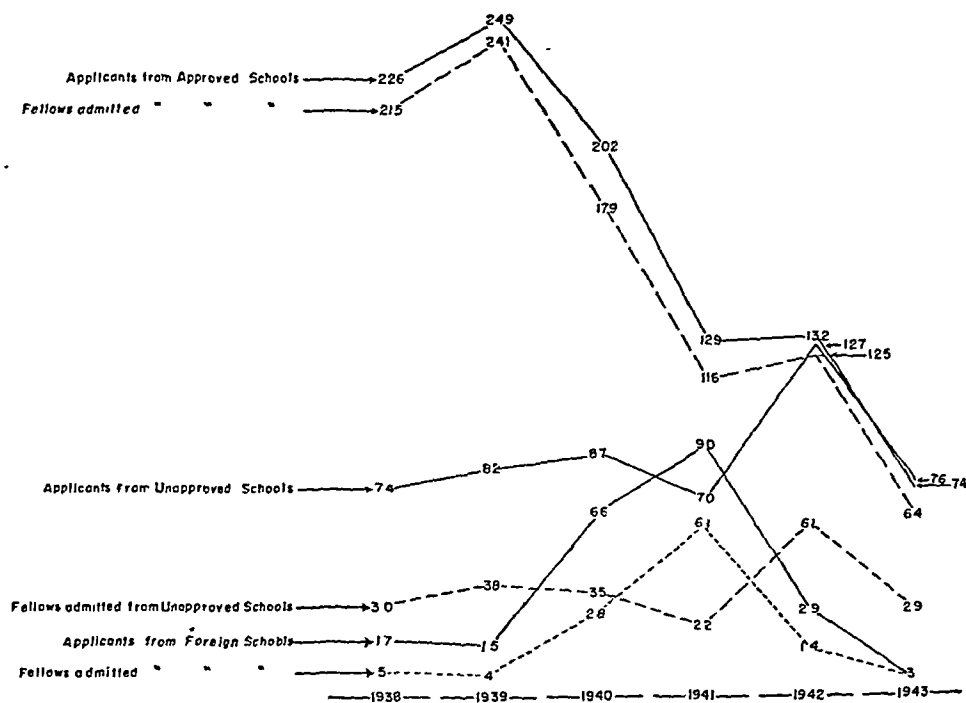


FIGURE 3. Applicants for and Admissions to Membership in the Massachusetts Medical Society Classified according to School of Graduation.

year wording as seemed best, admitting easily certain foreign trained physicians of assured reputability but holding back less well-known emigres from schools about which little was available.

Finally revised and accepted in May, 1942, the by-laws were clarified. It was voted that the diploma from a graduate of a foreign medical school be not approved unless he had possessed for at least five years a license to practice medicine in the United States or its territories.

It is, therefore, clear that there has been no departure of principle of the Society in the present by-law but only one of clarification of it, and that a considerable waiting period has been deemed advisable by this society before allowing applicants who are graduates of foreign medical schools to become fellows.

II. According to information from the Massachusetts Board of Registration in Medicine, beginning with 1939, all foreign-educated physicians must become citizens of the United States or have their registrations in this state revoked at the end of five years. It seems to the Committee on Membership that citizenship in the United States should be mandatory for fellowship in the Massachusetts Medical Society. It therefore seems clear that from this point of fact the five-year rule is necessary as it now stands.

physicians; and even with supervision, the testing period is short. On this point, therefore, membership in the Massachusetts Medical Society is not tantamount to for foreign educated physicians to allow them full scope in the practice of medicine in this state.

IV. Investigation of the medical caliber of graduates of foreign medical schools seemed advisable to the committee. In Figure 1 are shown the number of such applicants in each year from 1938 to 1943 who passed and failed the examinations by the Massachusetts Board of Registration in Medicine. The total figures are 309 passed and 403 failed. Of interest in this chart is that the greatest number of passed and registered applicants was in 1940, when 120 men were licensed. This group will be eligible under the present laws to become fellows of the Society within about a year or in approximately the same length of time necessary to alter or change the present by-law. Since 1940 it is obvious that there has been a steady decline in the number of foreign graduates passing the state-board examinations and therefore this rule should not be a great hardship.

It was also of interest to the committee to chart the experience of the Massachusetts Medical Society with graduates of foreign medical schools, taking as the index the censors' examinations for membership between 1938

1945 (Fig. 2). Again, in the last two years the number applicants has steadily fallen. In both Figures 1 and 2 to be noted that the ratio between passed and failed in class of applicants does not indicate a particularly high of medical education. This is further borne out by re 3, which charts this same ratio between number of applicants and number of applicants passed for fellowship the Massachusetts Medical Society in our three classifications. At the top is charted the curve between 1938 and 1945, inclusive, of graduates of approved United States schools. This graph indicates a high level of medical educational standards. The two lower pairs of curves represent, applicants of unapproved domestic schools and, second, applicants of foreign schools. Again, the ratio in these two groups between number of applicants and number passing the censors' examinations of the Massachusetts Medical Society shows quite a wide spread, unlike that of the approved schools, and a picture quite similar to each other. These groups of the unapproved domestic schools and graduates of foreign schools do not indicate a high level of medical educational standards.

* * *

To summarize, the Committee on Membership, through study of the history of the by-laws of the Massachusetts Medical Society, finds no departure of principle of the society in the present by-law, but only a clarification of it. It believes that a fellow of the Massachusetts Medical Society could be a citizen of the United States and a five-year period necessary in the case of foreign-born physicians to gain citizenship. Failing to become a citizen of the United States after licensure by this state means a mandatory revocation of license. The committee finds that foreign medical-school graduates as well as unapproved domestic-school graduates are allowed to practice medicine by the large percentage of hospitals, such privilege being a decision of the individual hospital trustees. Membership in the Massachusetts Medical Society is neither mandatory nor necessary for such hospital-practicing privilege. The committee also finds through study of the number of applicants of foreign medical-school graduates and graduates of unapproved domestic schools able to pass the examinations of the Massachusetts Board of Registration in Medicine and the censors' examinations of the Massachusetts Medical Society between 1938 and 1945, inclusive, that these substandard applicants show a markedly lower level of medical education than that of approved medical-school candidates for both of these examinations.

It is, therefore, the unanimous vote and recommendation of the Committee on Membership that the present by-law of the Massachusetts Medical Society, Chapter V, Section 2(b), remain unchanged.

Committee on Membership

HARLAN F. NEWTON, *Chairman*

JOHN E. FISH

PEIRCE H. LEAVITT

SUMNER H. REMICK

SAMUEL N. VOSE

Supervising Censors

WILLIAM H. ALLEN

H. QUIMBY GALLUPE

ALBERT E. PARKHURST

APPENDIX NO. 3

REPORT OF THE COMMITTEE ON INDUSTRIAL HEALTH

The Committee on Industrial Health has continued to work in close co-operation with the State Department of Public Health and with the Division of Occupational Hygiene of the State Department of Labor and Industries. In addition, your committee has been in contact with the Massachusetts Committee on Public Safety, the Massachusetts Safety Council, the Associated Industries of Massachusetts, the New England Conference of Industrial Physicians, the American College of Surgeons, the State Procurement and Assignment Service, and the Council on Industrial Health of the American Medical Association. Two members of the committee attended the annual meeting of the Council on Industrial Health of the American Medical Association, held in Chicago on February 14, 15 and 16.

The committee has kept up to date its register of physicians who might be interested in practicing industrial medicine.

The supply of physicians available for industrial medical service in Massachusetts continues in excess of the demand, however, and we have not succeeded in making more than a dozen placements during the year and a half that the register has been in operation. Of the original three hundred odd who registered with us, more than a third have requested, for various reasons, that their names be removed from the list. A few names have been added, but on the whole our experience has demonstrated that industrial health in Massachusetts does not lag for lack of medical placement. It is good to know that in these days of social shortages, some of which are being hung at the door of organized medicine.

Last fall the committee prepared a third industrial-health program, to be presented in Springfield. It was to have been similar to those previously held in Boston, but had to be canceled because a suitable meeting place could not be secured and also because the committee could not get evidence of sufficient local interest to support it.

During the winter the attention of the committee was directed to federal legislation calling for appropriations to state departments of labor for industrial health. We unanimously voted our emphatic disapproval of such appropriations, on the ground that matters of health should be administered by health departments, and that there should not be initiated in labor departments a duplication of work already well developed in most states by their health departments. Your committee considered that this was an important legislative matter, and was pleased to learn that the chairman of the Committee on Legislation was in hearty agreement with this opinion. With his knowledge, we communicated our views to the representatives from the Commonwealth of Massachusetts in Washington.

In its report on October 7, 1942, this committee stated that it was "most perplexed to know how to reach . . . those who are employed . . . in the small plants that are now rushing war production." The fact that three quarters of the workers are so employed gave this problem great urgency. It has been obviously impossible for the small plant to establish a real medical department, and it has been difficult for many of them to feel justified in employing full-time nurses; yet over the country as a whole the small plants were and still are providing the largest part of the industrial hazard to which our workers are exposed. A promising approach to this problem in Massachusetts has now been made by the activities of those who variously call themselves district nurses, visiting nurses or community-health nurses. Several of these groups in Massachusetts have already developed sufficient insight into industrial needs to offer a special part-time service to the small plants in their areas. These specialized services are now well beyond the experimental stage. They have been called to the attention of the industrialists,* and have so interested the Council on Industrial Health of the American Medical Association that it has signified its intention to visit the places where such services are in operation. In a paper read before the war session of the American College of Surgeons in Springfield on March 20, the plan was presented from the practitioner's point of view, and it was urged that physicians assume leadership in its future development; this paper is scheduled for publication in the June 8 issue of the *Journal*.

Throughout the Nation, both capital and labor have largely abated their traditional strife over hours and wages. But the striving continues and is frequently expressed in attempts to secure better working and living conditions, in the establishment of health services and benefits for employees, and in many things concerning which sound medical advice is pertinent and should be available. There has been created, in this period of unprecedented industrial activity, a somewhat artificial interest, which is above and beyond normal and valid interest in the promotion of industrial health. We should take advantage of this; the iron is hot, and now is the time to shape it. Industrial health can now be guided and established in plants where it was never thought of before and where, in the years to come, it may be difficult for it to gain another foothold.

The writer of this report regrets that time has not permitted him to submit it to his committee members. It contains no recommendations, and is respectfully presented as a report of continuing progress.

DWIGHT O'HARA, *Chairman*

*Whedee, R. F. Waltham's employee health plan for smaller industries. *Industry* Vol. IX No 7 April, 1944 P. 37.

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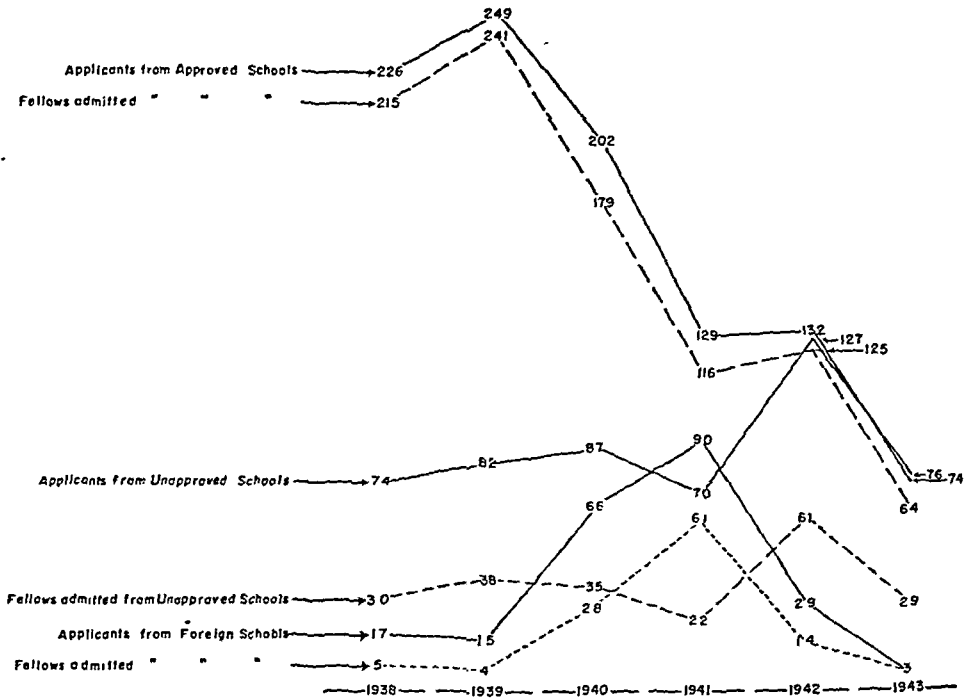


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is also agreed that the injured employee, if conscious, be offered two lists of physicians, — one a list of staff ors selected by the insurer and the other a complete list of the members of the hospital staff, including the courtesy list, — with the understanding that the employee has a free choice of any doctor on either of these lists. On the other hand, should the injured employee choose as his physician a doctor connected with some hospital other than the one in which he has been taken he may be removed without prejudice to that hospital, where the physician of his choice will care for him, provided that the other hospital is capable of rendering adequate care.

Your committee believes that it is impossible to prevent a certain number of these patients being taken to unaccepted hospitals and being cared for by men of limited ability, but that the solution of this part of the problem lies in an educational program designed to teach people the difference between recognized and unrecognized hospitals. The problem is not so simple as it seems at this time owing to the absence of many of the best men in the service and to the fact that in our places have been taken by men of considerably less ability in judgment.

There is one other arrangement that has recently been included that in some cases may obviate this difficulty. Through an agreement with the Blue Cross, an injured employee insured under the Blue Cross may be transferred from a ward to a semiprivate or private room and the difference in expense will be paid by the Blue Cross, making such an employee the private patient of the surgeon on duty or of a surgeon chosen by the employee.

It is further thought that freedom of choice of physician of the injured employee should at no time be interfered with. It is the desire of the chairman of the State Industrial Accident Board that a committee of this type be continued.

GORDON M. MORRISON
DAVID D. SCANNELL
DANIEL J. ELLISON, *Chairman*

APPENDIX NO. 6

REPORT OF THE COMMITTEE ON CANCER

The Committee on Cancer is able to report substantial progress.

Deeply conscious of its responsibility to the Society and to the victims of cancer dependent on the provisions for diagnosis and treatment maintained for their benefit by the Massachusetts Department of Public Health and encouraged by the action of the Council in its meeting on February 2, 1944, your committee felt impelled to make further efforts looking to an accord with the Department of Public Health in regard to the conduct of its state-aided cancer clinics.

This effort was initiated through the good offices of the president and president-elect of the Society and made possible by the co-operative attitude on the part of the Department of Public Health, as represented by the director of the Division of Adult Hygiene, who accepted an invitation to sit in with the committee at a meeting held in Boston on March 24, 1944.

In a report to the President-Elect, the director had pointed out that a plan for conducting the clinics which does not require the collection of fees from patients able to pay had been worked out for the Beverly Clinic and accepted by the Attorney General's office. This he termed Plan C.

This plan differs from the previous plan, which is now referred to as Plan A, in that it allows any citizen to consult the clinic without charge, but when the Commonwealth is billed for service only those medically indigent are included, since the Constitution does not allow the department to purchase services for other than "such persons as may be in whole or in part unable to support themselves." This results in the clinic receiving less money from the Commonwealth than it would otherwise but meets the objection to the clinic fee of \$10 raised by the Worcester and Beverly clinics, whereas it also sustains the Department of Public Health's policy that no citizen who desires to receive expert advice through group diagnosis by those particularly interested in malignant disease at the clinic can be refused, since they are not held to be ordinary charity clinics but part of a great effort to control such diseases in the public interest.

The director reported that the fees collected from patients in the three months of operation of Plan A have averaged \$2.34 per clinic per month. In the same period the average allotment to clinics from the State Treasury averaged \$213 per clinic per month.

He also explained to the satisfaction of all members present that the sums realized from fees charged patients did not really revert to the State Treasury but were pooled by the department and reallocated to the clinics through increased unit values, for their unrestricted use in maintaining the clinics and furthering the purpose of the clinics and of the cancer-control program.

The Director accepted the suggestion of the committee that the rules and regulations be revised (1) to clarify the paragraph relating to allocation of funds in the manner above explained and (2) to incorporate Plan C and offer it as optional to clinics not wishing to collect fees from persons able to pay but willing to conduct the clinics in all other respects in the manner prescribed by Plan A.

Your committee believes that with the above revisions the rules and regulations confer an added measure of local autonomy on the clinics and will therefore be more adaptable to local conditions while preserving the principle of group consultation service available to all cancer patients, as advocated by the American College of Surgeons, approved by the Department of Public Health and in harmony with the Cancer Law of 1926, as amended in 1943.

The Worcester Cancer Clinic Committee has agreed to accept the terms of Plan C as outlined above.

This committee therefore declares its readiness to recommend that the rules and regulations when so revised and given official sanction by the Public Health Council be approved by the Council of the Society.

Present were Drs. Balch, Simmons, Truesdale and Hunt. The vote was unanimous.

ERNEST L. HUNT, *Chairman*

* * *

The following are the revised regulations referred to in the report of the Committee on Cancer:

THE MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

The Cancer Clinic Regulations approved January 15, 1935, are hereby rescinded and the following substituted

FOREWORD TO CANCER CLINIC REGULATIONS

Whenever possible, all patients shall be referred to the clinic by the family physician, who may supply the clinic with the information requested on the referral card, and who may furnish the clinic with information as to the patient's ability to pay in whole or in part the regular clinic fee.

- 10 Referred patients will be returned for further diagnosis or treatment to the family physician whenever the physician so requests

CANCER CLINIC REGULATIONS

The Massachusetts cancer clinics are of two types: state cancer clinics and state-aided cancer clinics.

- 20 A state cancer clinic is a medical unit furnishing consultation service, diagnosis and treatment for persons suffering from precancerous conditions, suspected cancer, or cancer, "under the exclusive control, order and superintendence" of the State Department of Public Health. This type of clinic at present is held at Pondville and Westfield and could be held elsewhere (Plan B). A clinic under this plan would be administered by the Department of Public Health. The staff would be chosen and salaried by the department. Suitable accommodations, preferably at a hospital, would be selected and paid for by the department. There would be no local autonomy. This method would be expensive and with the present budget only a few clinics could be maintained.

- 30 A state-aided cancer clinic may be defined as a medical unit furnishing either consultation service alone, or consultation service, diagnosis and treatment, for persons suffering from precancerous conditions, suspected cancer, or cancer administered by an organized medical group through a committee, serving without compensation, and from whom the State purchases certain service for the care of "such persons who may be in whole or in part unable to support or care for themselves."

- 40 A committee composed of five or more physicians shall be appointed annually, either by the local medical society or by the staff of a hospital. This committee shall be known as the cancer-clinic committee. The local organized medical group, through its cancer clinic committee, may petition the State Department of Public Health to establish either a state cancer clinic (Plan B) or a state-aided cancer clinic (Plan A, C or D). If a state cancer clinic is requested by the local group and approved by the department, the cancer-clinic committee acts as an advisory body. If a state-aided cancer clinic is requested by the local group and approved by the department, the cancer clinic committee acts as an administrative body. The following rules and regulations apply to the state-aided cancer clinics.

The committee shall be responsible for all administrative matters pertaining to the clinic. These shall include the procurement of suitable quarters for the examination of the patients, preferably in

APPENDIX NO. 4

REPORT OF THE MASSACHUSETTS COMMITTEE ON PROCUREMENT AND ASSIGNMENT

At this meeting of the Council, your committee hoped to be able to close its accounts for the year with a certified statement of its labors. Unfortunately our books do not balance to the last penny, thus the best that we can offer is a description, which admittedly includes certain inaccuracies, of the present state of medical manpower in Massachusetts.

In 1942, the *American Medical Directory* listed 8085 names of doctors residing in Massachusetts. Among those included were practitioners known to be retired and also a number of interns and residents. During 1943 and until now in 1944, the Board of Registration in Medicine has licensed 457 new physicians. Theoretically, therefore, we should be called on to account for a total of 8542. Actually, biographical data have been assembled on 8922 doctors who have been in our midst at some time during the past two years. These names do not include men known to be deceased or retired but comprise physicians believed to have been active here either with temporary registrations or in some more permanent capacity. We always have a large floating medical population because of our reputation as a teaching center, and this probably accounts for the numbers of doctors with whom we have dealt. How many at any one moment were actually at work is not known.

In the group as a whole are 2900 commissioned officers. The studies of the War Participation Committee, as well as our own observations, justify the belief that Massachusetts so far has faced no significant medical shortage and indeed is unlikely to meet such misadventure in the future. Yet the withdrawal of approximately one third of our normal medical strength has brought to light certain aspects of the Procurement and Assignment Service that seem worthy of comment.

The usual age grouping used by the Procurement and Assignment Service divides doctors into four classes: those thirty-eight years old or under — young enough to be amenable to Selective Service persuasiveness; those thirty-nine to forty-four years old — of military interest but beyond the reach of Selective Service; those forty-five to sixty-four — of comparatively little military interest but of great use to civilian needs; and those sixty-five years old or over.

Of our 2900 officers, approximately two thirds are in the first group. They were easily procured because, if not in military service as medical students, they were reported to Selective Service when they did not apply for commissions shortly after they were declared available. The possibility of 1-A classification proved a powerful *vis a tergo*. Therefore, practically all young Massachusetts doctors are now accounted for. Besides those in service are 422 refused commissions by the Surgeons General, 243 declared essential, 75 women, 48 men honorably discharged from active service and 48 foreigners. All medical students in standard schools who are physically eligible for military service are in uniform. Only a few cases still remain to be classified.

The doctors more than thirty-eight years old who are in the Army, Navy and Public Health Service are the ones of whom the Society should feel most proud. They are the true medical volunteers of this war, men who soon learned that Selective Service would put no real pressure on them and who offered their services to their country, often at great personal loss, and solely from a deep sense of patriotism. The Society may well take pride in the fact that all but forty of these officers are of its membership.

The business of relocating physicians continues to be a baffling affair. So far as Massachusetts is concerned but few physicians have been relocated in regions short of medical talent. Your committee has received the impression that many older doctors have preferred, as their war contribution, to work harder than they should rather than to encourage newcomers. They have hoped thereby to hold open positions in their communities for the benefit of local younger men when they return from their military duties. This viewpoint is easily understood and a friendly one. So far, such a policy seems not to have been injurious either to medical or to public health. On the other hand, should replacements be needed in any part of the Commonwealth at any time, there are many young licensed practitioners ineligible for military service who are ready to fill any gap if only they receive encouragement to do so.

The 9-9-9 plan for interns and residents has now in operation long enough so that it moves with less ... than it did when first instituted. Hospitals on the whole less complaining than they were; young doctors educate acceleration appear able to assume clinical responsibilities with surprisingly good effect; residents developed under plan may be not quite so capable or so well trained as were, yet their judicious intermingling with staff of greater experience has made intramural hospital assignments reasonably satisfactory. On the whole the situation in Massachusetts seems to have clarified to a large extent and to have become better adjusted to conditions.

At the October meeting of the Council, the President mented on the tenuous thread by which the Massachusetts Procurement and Assignment Committee of the War Power Commission was related to the Society. Your committee has been thoroughly conscious of this and is grateful to the Council for the privilege of the pleasant relations has been maintained. Your committee also is grateful to Procurement and Assignment committees, which worked so industriously, to hospitals, to medical schools, the Board of Registration in Medicine, to the office of the secretary of the Society and indeed to all who have helped to make its efforts possible.

Henceforward, the work of the Procurement and Assignment Committee promises to be of much less magnitude heretofore and to deal with minor detail rather than broad interests. Problems connected with postwar plans however, are already assuming increasingly large proportions and deserve most careful study.

R. Fitz, Cha
H. M. C
E. L. K
D. O
W. H. P
B. P. Sw

APPENDIX NO. 5

REPORT OF THE COMMITTEE TO MEET WITH THE MILITARY ADVISORY COMMITTEE OF THE INDUSTRIAL ACCIDENT BOARD

This report is a follow-up in a matter on which a preliminary report was made one year ago.

This committee was appointed at the request of the Industrial Accident Board to recommend procedures for the medical care and surgical care of the injured worker might be improved. It was and still is the opinion of this committee that the surgical staffs of recognized hospitals, by and large, represent the men in any given community most able to cope with surgical conditions.

Our first procedure was to attempt to make these men willing to care for or handle industrial accident cases when they were on duty on ward service. To this end, through co-operation of the chairman of the Industrial Accident Board, it has now been agreed by all the insurance companies handling this type of business that the man rendering emergency treatment to an injured workman shall be paid for such treatment. In defining first-aid treatment it is said that emergency treatment ranges from simple aid to an extensive operation for the relief of a compound fracture. Reasonable charges submitted by any regular physician in this state will be honored. There shall be no change in the relation between the patient and the hospital staff physician as it now exists in the various hospitals of the Commonwealth. The problem of the surgeon on duty caring for an injured employee in the ward without being paid except for the emergency treatment cannot be solved by any method except the passage of an amendment to the law by the General Court providing for the payment for services or a reversal of the ruling previously made by the Supreme Court. It is the opinion of the committee that whereas surgeons on ward service render equally as able to both ward and private patients, it might be well to institute proceedings that would change this rather unfortunate state of affairs.

Payment will not be made for services rendered by interns or residents but for work actually done by surgeons recognized by a hospital, whether or not on duty. This we believe to be a step forward in the better care of the injured workman.

ENDIX NO. 8

STATEMENT OF DR. JACOB FINE

ask your indulgence in making the following statement relative to the report of the Committee on Membership. I all refer to the issues discussed in this report in the order in which they are presented.

The Committee on Membership states that, according to the Board of Registration in Medicine, 309 graduates of foreign medical schools were licensed in Massachusetts from 1933 to 1943. In the 1942 edition of the *American Medical Directory*, the Boston Committee on Medical Emigrés could find more than 165 names of men in this class of licensed physicians who were in actual practice between the years 1933 and 1942. The discrepancy between these figures may therefore be due to the fact that only 165 are in actual practice. The Boston Committee endeavored several times without success to obtain full data from the Board of Registration. In any case it is not clear why this discrepancy would make it difficult for the Committee on Membership to evaluate the remainder of my statement, which deals mainly not with numbers but with the question whether or not the experience of the Society, before or since adoption of the five-year exclusion provision, justifies continuation of this provision.

The Committee on Membership, in reviewing the history of admission of foreign physicians, states, "The general policy operated fairly well until an increasing number of these physicians began to infiltrate Massachusetts." It further states, "No one knew how good an education such people had received." I do not believe that the Committee on Membership means to question the performance of the Board of Registration in Medicine on this point, for the Board certainly knew in every instance what school or schools were attended and the number of hours of instruction received in each course. The report of the Committee on Membership states that according to the chairman of the Committee on Medical Education, it is almost impossible to evaluate the medical education in foreign schools, particularly in Europe. This is to some extent true for those who graduated from continental schools after 1933, but it is certainly not true for those schools before 1933, and the great majority of the medical emigrés graduated before that year.

The report goes on to state, "The by-laws were rewritten in 1939 so as to require that a foreign physician, to be eligible for membership in the Society, must have practiced for a minimum of five years and be recommended by a number of his colleagues who were fellows." I shall quote the next paragraph in the report in full:

The expression "must have practiced for a minimum of five years" was evidently purposely loose; it might mean practice anywhere—indeed including internship as practice—or might be interpreted to mean a minimum of five actual years of practice within the confines of Massachusetts. This was done so that the Committee on Medical Education and Medical Diplomas might interpret the five-year wording as seemed best, admitting easily certain foreign-trained physicians of assured repute but holding back less well-known emigrés from schools about which little was available.

But the very next sentence of the report continues without further explanation as follows, "Finally revised and accepted in May, 1942, the by-laws were clarified." To wit, that the foreign physician shall not be approved for membership unless he had possessed for at least five years a license to practice medicine in the United States or its territories. This the Committee on Membership emphasizes is only a clarification, and not a departure in principle. I submit, with due respect to the committee, that this is not a clarification and that it is indeed a departure in principle, since no foreign physician, however competent or eminent, may now join the Society until five years after he has received

a license to practice in the United States, whereas up to 1932 he could and did join the Society before five years following licensure. It is pertinent at this point to ask whether the experience of the Society between 1939 and 1942, when the five-year exclusion provision was adopted, was such as to require this so-called "clarification." The 1939 amendment, as the report states, was written so as to allow the Committee on Medical Education and Diplomas latitude in judging the admissibility of candidates. What the latter committee had to do was clear enough. Is there any evidence that physicians of dubious qualifications were being certified for membership during the years 1939 to 1942? No such evidence has been offered. If it had been offered, it is not likely that the Committee on Medical Education would have stood its ground in unanimously opposing the five-year exclusion provision.

In the second section of its report the committee notes that the Board of Registration in Medicine requires that the recipient of a license shall become a citizen five years after receipt of the license. The Committee on Membership, however, is of the opinion that, although the recipient of a license is allowed to practice medicine before he becomes a citizen, he should not be admitted to the Society until after he becomes a citizen.

In the third section the Committee on Membership states that the five-year rule will work a hardship on certain foreign-educated physicians, but believes that this is a rare occurrence. Unfortunately this is not so rare an occurrence as the Committee on Membership believes. How can the five-year rule work a hardship? The Committee on Membership like the Boston Committee on Medical Emigrés, is evidently aware that in some towns and cities of this state, the foreign physician is informed that he cannot bring his patients to a hospital because he is not a member of the Massachusetts Medical Society. He must therefore practice medicine for not less than five years before this restriction can be removed. It is not especially helpful to state that American citizens trained abroad have no difficulty in getting hospital appointment, or that many of the best hospitals in this state allow courtesy staff privileges to foreign physicians. Although it is true that for such privileges membership in the Society is not necessary or mandatory, the fact that it is recommended—and no one will question the wisdom of this recommendation—constitutes a basis for exclusion, whenever hospital authorities choose to do so.

In the fourth section the committee states that the five-year provision will not affect foreign physicians who were licensed in 1940 or before, because all of them will have become citizens by 1945, the earliest date possible for removal of the restriction. But I think we shall all agree that the Society is more concerned with whether or not restriction is correct in principle, than with what effect it may have for the moment on a particular group of physicians licensed in any given year. By-laws are not temporary provisions—they embody what are intended to be lasting principles of ethics, standards and procedure.

The committee finally makes the observation that, because foreign physicians did not do substantially better on the Board examination than graduates of unapproved domestic schools, the medical-education standards of European schools are not on a high level and that consequently the five-year exclusion provision is justified. As already stated, the majority of the foreign physicians graduated before 1933. Since the Committee on Membership presumably does not intend to suggest that European medical schools were generally substandard before 1933, the showing of these foreign physicians in the examinations must be explained on a different and quite understandable basis, that is, age and language. We need only to consider whether an average graduate of an American Grade A school, around forty years of age, perhaps practicing in a special field at that, would do better in a licensing examination in a foreign language in a foreign country, a year or so after arriving there, following one or more years out of practice and burdened by a harrowing recent past and a host of immediate difficulties.

50 a hospital, and the appointment and responsibility for the medical personnel, nurses, follow-up workers and clerical help of the clinic. Follow-up of cancer patients until death, and precancerous patients until the precancer is removed, and the maintenance of a uniform record system are required.

The committee shall make arrangements with the hospital in which the clinic meets to furnish examination rooms, instruments, diagnostic x-rays and other essential equipment and supplies.

60 At least three physicians should be present at each clinic session and shall preferably be a surgeon, a radiologist and a pathologist. If available, representatives of the various specialties shall be on call. A nurse is to be in attendance at all clinics.

A clerical worker shall have charge of the clinic files and furnish such reports through the district health officer as may be requested. Uniform record forms will be supplied to the clinics.

Each clinic is to employ a "cancer clinic follow-up worker." This individual will attend to the follow-up and related duties of the clinic. In some of the smaller clinics it may be well, for purposes of economy, to combine the duties of the follow-up worker and the clerical worker. The minimum qualifications for the follow-up worker shall consist of some previous exposure to medical and social problems, as well as some knowledge of the medical and social resources available in the community.

When a problem arises which calls for advice from a medical social worker, unless the cancer-clinic follow-up worker is a trained medical social worker approved by the department, a request for aid should be sent to the local district health officer.

All new appointments of clinic personnel shall be subject to the approval of the department. The department reserves the right to approve on a temporary basis the appointment of personnel who do not meet the minimum qualifications, and to approve other changes in the clinic, during the war emergency.

80 The local cancer clinic committee which petitions for a state-aided clinic shall designate whether it desires to function under Plan A, C or D. These plans have been promulgated in order to give each individual clinic the maximum amount of local autonomy consistent with the Constitution of Massachusetts, the Cancer Act of 1926, as amended by the Act of 1943, and the policies of the Department of Public Health.

90 Plan A. The department will pay for services rendered by the clinic for "such persons as may be in whole or in part unable to support or care for themselves." Each clinic shall determine which individuals are "in whole or in part unable to support or care for themselves." Clinics in hospitals which do not have a prescribed form for determining medical indigency and clinics in those hospitals whose method is not approved by the department shall adopt the department method. This consists of a personal interview with the individual by the admitting office. Due care in selection of the admitting officer is of utmost importance. All individuals coming to the clinic who do not fall into the class of "such persons as may be in whole or in part unable to support or care for themselves" will reimburse the clinic for services. The standard fee shall be \$10, which will include all routine and subsequent follow-up service. This does not include the services of the physicians of the clinic staff which are gratuitous or certain hospital services, such as x-ray examinations, which must be paid by individuals in this class at established hospital rates. Individuals unable to pay \$10 but able to pay some fraction of that amount may do so.

100 Plan C. This plan is somewhat similar to Plan A. All patients seeking consultation service are examined at the clinic and receive advice irrespective of their financial status but the Commonwealth is only billed for "such persons as may be in whole or in part unable to support or care for themselves" and no fee is collected from any individual.

Plan D. Under this plan a clinic may be conducted with other arrangements for payments or for management, or both, provided the arrangement is constitutional, conforms to the legislative mandate, contains local autonomy, is not contrary to public-health practice, and conforms to the American College of Surgeons' plan for making group diagnosis available to all.

120 In order to make the payments equitable for all clinics differing in size and services rendered, the following procedure for payments has been adopted:

Each clinic shall submit monthly a list of services rendered the preceding month. Unit values have been determined for the ordinary services rendered by a cancer clinic. These are termed service units. The service units are totaled for each clinic by the department and then converted into payment units. The payment units of all clinics, with the exception of those which, because of balances due to donations of clubs, individuals, Community Chest, legacies and other sources, do not need current payments, are totaled. The money available for the clinics for a given month is divided by this figure to determine the monetary value of a payment unit. This figure multiplied by the number of payment units for a given clinic minus the money received from patients who pay all or part of the \$10 fee furnishes the amount of clinic payment to be made by the Commonwealth. In this way the Commonwealth pays for none of the services to individuals who can pay for themselves and only for a part of the services of "such persons who may be in whole or in part unable to support or care for themselves," as both physicians

140 and hospitals contribute materially to all groups. After the department has determined the value of the payment unit, an invoice shall be sent to the clinic for signature. On both the monthly report and the invoice, the following certification under penalty of perjury shall be made: "The clinic is billing the Commonwealth only for the services rendered, to the best of our knowledge and belief, to such persons who may be in whole or in part unable to care for themselves."

Itemized accounting of clinic expenditures is required under Plan B, might be required under Plan D, but would not be required under Plans A and C in which the relation between the department and the clinic is that of purchaser and seller of services. The department, however, suggests that if any clinic operating under Plan A or C accumulates a balance due to donations of clubs, individuals, Community Chest, legacies and other sources, such monies be expended in improving the clinic, furthering cancer education or some other form of cancer control.

If major changes in the management of a clinic are contemplated, the approval of the Department of Public Health should be obtained.

The Department of Public Health reserves the right to hire representative make regular inspections of the clinics and make suggestions for improved service. It may cease purchasing service of a clinic which fails in its obligations to the public.

When a clinic ceases to sell service to the Commonwealth, or by a vote of the local group which originally sponsored it, or by vote of the Department of Public Health, it is the responsibility of the department to follow the cancer patients previously seen at clinic, until death. Arrangements must be made either with the clinics, district health units, voluntary agencies or the state cancer-clinic committee, to see that this is done.

170

SERVICE UNITS

TYPE OF SERVICE	VALUE IN CENTS
New case	10
Return case	5
Special consultation	5
Gastrointestinal series	20
Other x-rays	10
Complete blood examination	1
Proctoscopic examination	1
Cystoscopic examination	2
Biopsy	3
Social service:	
Home visit	6
Office consultation	2
Telephone and correspondence	1
Transportation of patients	4

APPENDIX NO. 7

REPORT OF THE COMMITTEE ON POSTWAR LOAN FUND

The Committee on Postwar Loan Fund approves in principle the desirability of raising funds from which loans can be made to members of the Massachusetts Medical Society who, having served in the Armed Forces, on discharge from active duty may be in need of immediate financial assistance.

The committee recommends:

That these funds shall be raised by an added annual assessment of \$10 for the duration of the war unless otherwise modified by future action of the Council. This added annual assessment of \$10 is to be levied on all members of the Society not having served in the armed forces during this war.

That payment of the Postwar Loan Fund assessment by members of the Massachusetts Medical Society while in the armed forces be entirely optional.

That payment of the Postwar Loan Fund assessment by members of the Massachusetts Medical Society following discharge from active duty also be entirely optional.

That the amount of loan granted be left to the discretion of the board or committee appointed by the President.

That just enough interest be charged — not to exceed 2 per cent — to cover carrying charges and remind the member obtaining a loan of his obligation.

That no endorsers be required.

That loans shall be limited to a period of twelve months subject to renewal at the discretion of the board or committee appointed.

That only those who were members, in good standing, of the Massachusetts Medical Society on the date they entered the armed forces shall be permitted to borrow from this fund.

That, to inform members of the Society in the armed forces of the availability of this fund, information be printed in the *New England Journal of Medicine*. There shall also appear in a box on the cover of the *Journal* an announcement calling attention of the members to the article on the inside page.

That form letters shall be sent to the members in the armed forces notifying them of the existence of this fund.

That form letters shall be sent out to the other members of the Society with the annual bills for dues bringing to their attention the existence of this fund and its purpose.

That the fund shall be administered from the headquarters of the Massachusetts Medical Society.

That the president of the Massachusetts Medical Society appoint a committee or board of five members, to include the treasurer and the secretary of the Society and the present chairman of the Committee on Postwar Loan Fund, to administer this fund.

GEORGE LEONARD SCHATZ, Chairman

APPENDIX NO. 8

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The report goes on to state, "The by-laws were rewritten in 1939 so as to require that a foreign physician, to be eligible for membership in the Society, must have practiced for a minimum of five years and be recommended by a number of his colleagues who were fellows." I shall quote the next paragraph in the report in full:

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Plan A. The department will pay for services rendered by the clinic for "such persons as may be in whole or in part unable to support or care for themselves." Each clinic shall determine which individuals are "in whole or in part unable to support or care for themselves." Clinics in hospitals which do not have a prescribed form for determining medical indigency and clinics in those hospitals whose method is not approved by the department shall adopt the department method. This consists of a personal interview with the individual by the admitting office. Due care in selection of the admitting officer is of utmost importance. All individuals coming to the clinic who do not fall into the class of "such persons as may be in whole or in part unable to support or care for themselves" will reimburse the clinic for services. The standard fee shall be \$10, which will include all routine and subsequent follow-up service. This does not include the services of the physicians of the clinic staff which are gratuitous or certain hospital services, such as x-ray examinations, which must be paid by individuals in this class at established hospital rates. Individuals unable to pay \$10 but able to pay some fraction of that amount may do so.

Plan C. This plan is somewhat similar to Plan A. All patients seeking consultation service are examined at the clinic and receive advice irrespective of their financial status but the Commonwealth is only billed for "such persons as may be in whole or in part unable to support or care for themselves" and no fee is collected from any individual.

Plan D. Under this plan a clinic may be conducted with other arrangements for payments or for management, or both, provided the arrangement is constitutional, conforms to the legislative mandate, contains local autonomy, is not contrary to public-health practice, and conforms to the American College of Surgeons' plan for making group diagnosis available to all.

In order to make the payments equitable for all clinics differing in size and services rendered, the following procedure for payments has been adopted:

Each clinic shall submit monthly a list of services rendered the preceding month. Unit values have been determined for the ordinary services rendered by a cancer clinic. These are termed service units. The service units are totaled for each clinic by the department and then converted into payment units. The payment units of all clinics, with the exception of those which, because of balances due to donations of clubs, individuals, Community Chest, legacies and other sources, do not need current payments, are totaled. The money available for the clinics for a given month is divided by this figure to determine the monetary value of a payment unit. This figure multiplied by the number of payment units for a given clinic minus the money received from patients who pay all or part of the \$10 fee furnishes the amount of clinic payment to be made by the Commonwealth. In this way the Commonwealth pays for none of the services to individuals who can pay for themselves and only for a part of the services of "such persons who may be in whole or in part unable to support or care for themselves," as both physicians and hospitals contribute materially to all groups.

After the department has determined the value of the payment unit, an invoice shall be sent to the clinic for signature. On both the monthly report and the invoice, the following certification under penalty of perjury shall be made: "The clinic is billing the Commonwealth only for the services rendered, to the best of our knowledge and belief, to such persons who may be in whole or in part unable to care for themselves."

Itemized accounting of clinic expenditures is required under Plan B, might be required under Plan D, but would not be required under Plans A and C in which the relation between the department and the clinic is that of purchaser and seller of services. The department, however, suggests that if any clinic operating under Plan A or C accumulates a balance due to donations of clubs, individuals, Community Chest, legacies and other sources, such monies be expended in improving the clinic, furthering cancer education or some other form of cancer control.

If major changes in the management of a clinic are contemplated, the approval of the Department of Public Health should be obtained.

The Department of Public Health reserves the right to employ representative make regular inspections of the clinics and make suggestions for improved service. It may cease purchasing service to a clinic which fails in its obligations to the public.

When a clinic ceases to sell service to the Commonwealth, by a vote of the local group which originally sponsored it, or by vote of the Department of Public Health, it is the responsibility of the department to follow the cancer patients previously seen in the clinic, until death. Arrangements must be made either with clinics, district health units, voluntary agencies or the cancer-clinic committee, to see that this is done.

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SERVICE UNITS

TYPE OF SERVICE	VALUE IN CTS
New case	10
Return case	5
Special consultation	5
Gastrointestinal series	20
Other x-rays	10
Complete blood examination	3
Proctoscopic examination	1
Cystoscopic examination	2
Biopsy	3
Social service:	
Home visit	6
Office consultation	1
Telephone and correspondence	1
Transportation of patients	4

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APPENDIX NO. 7

REPORT OF THE COMMITTEE ON POSTWAR LOAN FUND

The Committee on Postwar Loan Fund approves in principle the desirability of raising funds from which loans can be made to members of the Massachusetts Medical Society who, having served in the Armed Forces, on discharge from active duty may be in need of immediate financial assistance.

The committee recommends:

That these funds shall be raised by an added annual assessment of \$10 for the duration of the war unless otherwise modified by future action of the Council. This added annual assessment of \$10 is to be levied on all members of the Society not having served in the armed forces during this war.

That payment of the Postwar Loan Fund assessment by members of the Massachusetts Medical Society while in the armed forces be entirely optional.

That payment of the Postwar Loan Fund assessment by members of the Massachusetts Medical Society following discharge from active duty also be entirely optional.

That the amount of loan granted be left to the discretion of the board or committee appointed by the President.

That just enough interest be charged — not to exceed 2 per cent — to cover carrying charges and remind the member obtaining a loan of his obligation.

That no endorsers be required.

That loans shall be limited to a period of twelve months subject to renewal at the discretion of the board or committee appointed.

That only those who were members, in good standing of the Massachusetts Medical Society on the date they entered the armed forces shall be permitted to borrow from this fund.

That, to inform members of the Society in the armed forces of the availability of this fund, information be printed in the *New England Journal of Medicine*. There shall also appear in a box on the cover of the *Journal* an announcement calling attention of the members to the article on the inside page.

That form letters shall be sent to the members in the armed forces notifying them of the existence of this fund.

That form letters shall be sent out to the other members of the Society with the annual bills for dues bringing to their attention the existence of this fund and its purpose.

That the fund shall be administered from the headquarters of the Massachusetts Medical Society.

That the president of the Massachusetts Medical Society appoint a committee or board of five members, to include the treasurer and the secretary of the Society and the present chairman of the Committee on Postwar Loan Fund, to administer this fund.

GEORGE LEONARD SCHAFF, Chairman

there were moist basal rales and respiratory rales throughout the lungs. Her condition became progressively worse, and she died on the sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: If we say that this woman obviously died of Bright's disease, no one can refute that we have to do better than that because there is more than one type of Bright's disease. I think that we may assume that she died of azotemia or uremia resulting from renal failure, in turn resulting in some kind of renal nephropathy with infection toward the end, and left ventricular failure, due either to her disease or perhaps to overtreatment. So, she apparently had mild diabetes.

The differential diagnosis as I see it is really one of what kind of kidney lesion she had, and what kind of infection. Perhaps we should take up the latter first. I can see no evidence of infection anywhere except in the urinary tract. The lung picture does not sound to me like an infectious process. She had pus in the urine, and therefore I think that she probably had a urinary-tract infection and I will let it go at that for the moment.

The type of kidney lesion is an interesting subject for differential diagnosis. One might ask, Did she die of one of the more usual forms of chronic kidney lesion to which we may give the clinical name of Bright's disease, or did she have a rarer type of nephropathy? We have to go into all that to suppose to satisfy the requirements of these exercises, but I think from the practical point of view this is of little importance, as both Dr. Thorn and Dr. Cutler have emphasized that the physiologic abnormalities are much more important to identify and treat than is the precise nature of the anatomic lesion.

This patient had acidosis and she was hyperglycemic. She may have had a high threshold for sugar. She had a low blood sodium. These were the things that they had to treat. They gave fluid because of the dehydration, and sodium lactate because of the acidosis. I do not know why they gave 5 per cent glucose in water, because the sodium was low. The sodium racemic lactate was also given because of the acidosis. I do not know how much of the substance 40 cc. represents.

Was this chronic glomerulonephritis? It could have been, but I have a notion that it was not, and I am not going to give any reason. It could, of course, have been a vascular nephritis with malignant hypertension, and I suppose it could have been a chronic pyelonephritis. In their monograph about pyelonephritis Weiss and Parker¹ mention that it is often associated with severe hypertension, that retinopathy may occur, as in this case, that there is often a terminal infection with ventricular failure, as in this case, and that the hypertension may progress after the renal disease is in a healed stage.

This patient may not have started off with pyelonephritis, but may have had some other chronic kidney disease, picking up an acute pyelitis not long before death. I do not know how anyone can tell whether it was pyelonephritis from the start or something else to which pyelonephritis was later added. I rather favor the addition of an acute pyelonephritis toward the end because the infection seems to have been recent. Although the diabetes had been mild for a long time, it became worse toward the end. Its aggravation may have been the result of infection, and the change may have been the last straw that broke the camel's back and precipitated failure in kidneys that were chronically diseased.

I have mentioned four possibilities, and I think that we should now turn our attention to the more specialized nephritides. I do not know much about it but the fact that she had diabetes makes me think of the special kind of lesion that one gets with diabetes that is called "intercapillary glomerulosclerosis." I looked up Newburger and Peters² on that subject to find out the clinical manifestations that one can expect, and found that they described this disease as running a chronic course; many of the features of malignant hypertension may be present, including hypertensive retinopathy, perhaps albuminuria and marked evidence of renal failure toward the end. They also say, and it fits this case perfectly, that the diabetes is often mild, usually requiring little or no insulin for control except when an infection supervenes. In none of their cases did the diabetes tend to influence the progress of the disease. All I can say is that this case in most of its aspects fits that possibility fairly well. That does not mean, however, that it is the correct diagnosis.

I did in passing think of nephropathy due to hyperparathyroidism, but this patient did not have hyperparathyroidism according to the evidence, so we can throw that out. I do not see how it could have been nephropathy due to lymphoma, and I shall also throw that out.

We come finally to the lobular mass in the right flank. If I knew that the man who examined the patient really knew that he was feeling a mass it would help me a great deal. I have to approach the problem on the basis that he did feel one. Therefore, with chronic nephropathy and renal failure, one is bound to consider the possibility that this was a case of congenital polycystic kidneys with renal failure. I believe, barring the diabetes, that that diagnosis would cover everything in this record. Polycystic kidneys usually make themselves evident early in childhood, as I understand it. If the disease does not turn up then, it is apt to appear later in life, as in this case. Weiss and Parker make the intriguing statement that polycystic kidneys, hypertension and renal tuberculosis are often complicated by pyelonephritis. Perhaps the sequence of events here was that the patient had

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30301

PRESENTATION OF CASE

A sixty-three-year-old housewife entered the hospital because of tiredness, exhaustion and weakness.

The patient was apparently well until eight years prior to entry, when she was told that she had high blood pressure. She had had frequency of urination and "trouble with her eyes" but otherwise remained asymptomatic until eight months before admission, when, following the death of her sister, she felt run down and exhausted. Her appetite became poor. About one week before entry she was seen by her physician, who found retinal exudate and hemorrhages, with a slightly enlarged heart and a blood pressure of 220 systolic, 120 diastolic. Urinalysis revealed a specific gravity of 1.018 and a +++ test for albumin with many pus cells and bacteria in the sediment. She was advised to take 1 gm. of sulfadiazine daily, but because of anorexia, nausea, vomiting and diarrhea, she took only 0.5 gm. daily. She was unable to take anything by mouth. She developed slight fever on the day before entry. She had had no headaches, shortness of breath, edema, orthopnea, chest pain, palpitation or chills.

Eight years before admission she had an ulcer on the right shin that healed very slowly. At that time she was found to have mild diabetes, which was controlled by regulation of diet. Urine tests performed by the patient three times daily had remained pale green. She had recently developed polydipsia. She had lost 15 pounds in weight in one year.

One sister had hypertension and died of cerebral hemorrhage. One brother died of "shock." Her mother died at eighty years of age of cerebral hemorrhage, and her father at sixty-seven of acute Bright's disease. There was no family history of diabetes. She had one son who was living and well.

Physical examination showed a well-developed, dehydrated, weak, apathetic woman showing evidence of recent weight loss. The oral mucosa was dry. The retinas showed marked arterial narrowing, tortuosity and arteriovenous nicking; on the right side several hemorrhages and an exudate were seen. The nasal half of the left optic disk was indistinct. The left border of cardiac dullness was just to the

right of the midclavicular line. The sounds, of good quality and regular. The aortic sound was greater than the pulmonic. The lungs were clear. The abdomen was normal. Arterial pulsations were poor in the lower extremities, but no color or temperature changes were noted.

The blood pressure was 156 to 140 systolic, 100 to 90 diastolic. The temperature was 102°F., the pulse 120, and the respirations 25.

Examination of the blood showed a white count of 15,200, with 84 per cent neutrophils. Hemoglobin was 10.1 gm. per 100 cc. The urine was alkaline, with a specific gravity of 1.010. There was a ++ test for albumin, but no sugar, diacetic acid or acetone. The sediment contained 10 red cells and 100 white cells, with rare clumps, per high power field. A urine culture gave no growth. The fasting blood sugar was 286 mg. per 100 cc., and the nonprotein nitrogen 135 mg. The carbon dioxide combining power was 10.3 millimol. per liter, and the sodium 129 milliequiv.

The patient was given 1500 cc. of 2.5 per cent glucose in physiologic saline solution intravenously followed by 1000 cc. of the same solution to which an ampule of sodium lactate had been added. Two grams of triple bromides was given immediately and daily for two days thereafter. Following the two intravenous solutions she still seemed dehydrated, an uremic odor was noted in the breath; the vomiting apparently subsided. On the second and third hospital days she received daily 1000 cc. of 5 per cent glucose in water to which 40 cc. of sodium race lactate had been added, followed by 1500 cc. of 5 per cent of dextrose in 0.3 normal saline solution as well as thiamine chloride, ascorbic acid and riboflavin intravenously.

On the second hospital day the nonprotein nitrogen was 165 mg. per 100 cc., and the sugar 278 mg. The urine output on the third hospital day was 1000 cc. on an intake of 3000 cc. Urinalysis remained essentially as before. On the afternoon of the third hospital day, following the administration of an intravenous fluid, she began to cough, complained of pressure in the chest and became drowsy and extremely apprehensive. She vomited with every intake by mouth, and her color became poor. The lungs showed many basal rales. She was placed in an oxygen tent. Twelve hours later she was still cyanotic but not dyspneic; there were rhonchi in the trachea and a few rales and squeaks in the lungs. She was given 8 mg. of Cedilanid intravenously, followed by 11 mg. (1/6 gr.) of morphine sulfate, followed by 0.1 gm. of digitalis daily. In the next few hours she improved temporarily and the vomiting subsided. The abdomen became quite distended, and the examiner felt a questionable lobulated mass in the right flank. There was no peripheral edema. Later that day she again became drowsy and developed uremic frost in the nose; the respirations became shallow and rapid. The heart sounds were w

*On leave of absence.

there were moist basal rales and respiratory rales throughout the lungs. Her condition became progressively worse, and she died on the sixth fatal day.

DIFFERENTIAL DIAGNOSIS

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congenital polycystic kidneys that functioned well until eight years before her terminal illness; the kidneys then became incompetent and finally picked up an infection, the diabetes got worse, and she died.

All I can do is make these two suggestions, which I put on a par, because I do not know whether or not a mass was really felt. If it was, I would favor polycystic kidneys. If there was no mass, I would incline toward intercapillary glomerulosclerosis. It may have been neither of these — just a more ordinary kind of chronic nephritis.

DR. ALLAN M. BUTLER: Dr. Means asked about the amount of racemic sodium lactate in 40 cc. That

ANATOMICAL DIAGNOSES

Congenital polycystic kidneys and liver.
Acute pyelonephritis.
Bacteremia (colon bacillus).
Pulmonary edema.
Bronchopneumonia.
Cardiac hypertrophy, hypertensive type.
Coronary sclerosis, severe.
Myocardial fibrosis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this patient showed a pair of polycystic kidneys, with



FIGURE 1. Photograph of Kidneys.

is difficult to answer because it does not give the concentration. The commercial ampules, however, contain 40 cc. of 1 molar sodium lactate, which has the same quantity of sodium that is contained in approximately 250 cc. of physiologic saline solution.

CLINICAL DIAGNOSES

Essential hypertension.
Pyelonephritis.
Hypertensive coronary heart disease.
Mild diabetes.
Congestive heart failure, terminal.

DR. MEANS'S DIAGNOSES

Congenital polycystic kidneys or intercapillary glomerulosclerosis.
Acute pyelonephritis, recent.
Uremia.
Diabetes mellitus.
Left ventricular cardiac failure.

together weighed 700 gm. (Fig. 1). A moderate amount of renal parenchyma was still present, but a large portion of it certainly was replaced by congenital cysts. In addition there was an acute pyelonephritis, characterized by large foci of polymorphonuclear and eosinophilic infiltration. A post-mortem blood culture yielded colon bacilli, which probably arose from the pyelonephritis. For acute infection were present in other organs including the liver, secondary to the terminal bacteremia.

There were also congenital cysts in the liver. It occurs in about 20 per cent of the cases of polycystic kidneys. In addition to the large cysts there were grayish-white, moderately firm areas, 2 to 3 in diameter, throughout the liver that in gross dissection resembled metastatic carcinoma. These proved microscopically to be foci of aberrant bile ducts, a condition that may be associated with congenital cystic disease of the liver. Some of these ducts were dilated and filled with fluid and polymorphonuclear leukocytes. Others were suggestive

use cholangioma, but there was no bile in any of these small nodules and they are best interpreted as part of the congenital process within the liver. The heart was enlarged, weighing 500 gm., and showed large areas of scarring throughout, due to severe coronary sclerosis. There was also severe pulmonary edema and early bronchopneumonia. We found no anatomic evidence of diabetes; the islets of Langerhans were normal.

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CASE 30302

PRESENTATION OF CASE

A forty-seven-year-old housewife entered the hospital for study.

The patient had been in apparent good health, except for mild indigestion and intolerance for fatty and fried foods of many years' duration, until five or six months before entry when she noted a feeling of bloatedness, considerable eructation and passage of gas by rectum. She had no nausea or vomiting but voluntarily limited her intake of food. About five months before admission she had a feeling of constricting pressure in the right upper quadrant when wearing a girdle. About the same time she noted a hard mass in the right upper quadrant. The mass gradually became larger, and one week before entry she consulted a physician, who advised hospitalization.

Four days prior to entry the patient had an attack of severe pain over the lower part of the mass, which was tender. She became nauseated and vomited, the vomitus consisting of bile-stained material without blood. She had been constipated. The pain persisted and she was brought into the Emergency Ward. She had lost about 20 pounds since the onset of her illness.

Physical examination showed a well-developed, slightly undernourished woman in no discomfort. The heart and lungs were normal. There was a firm, tender, irregular mass in the midepigastrium extending to the right side of the abdomen and in the midline to 2 cm. below the umbilicus. A questionable liver edge was palpated in the right flank and seemed to be attached to the mass. The mass moved slightly with respiration. Its lower edge was more or less freely movable, the upper part was firmly attached and immobile. The mass was dull to flat on percussion. Peristalsis was normal. No other masses or tenderness was elicited. Vaginal and rectal examinations were negative except for a feeling of fullness in the cul-de-sac.

The blood pressure was 116 systolic, 70 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

The red-cell count was 3,780,000, with 10.5 gm. of hemoglobin. The white-cell count was 5700, with 66 per cent neutrophils. The urine was normal. A blood Hinton test was negative. Three stool examinations were guaiac negative, but one examination gave a +++ test. The blood sugar was 113.5 mg. per 100 cc. The nonprotein nitrogen was 19 mg. per 100 cc., and the chloride 101 milliequiv. per liter. A van den Bergh test was normal. The prothrombin time was 27 seconds (normal, 18 to 20 seconds). The serum protein was 7.01 gm. per 100 cc., with 4.27 gm. of albumin and 2.74 gm. of globulin. A cephalin flocculation test was negative in twenty-four hours, and + in forty-eight hours.

An x-ray examination of the chest was negative. A Graham test failed to visualize the gall bladder. No stones were seen. An intravenous pyelogram showed normal kidneys, pelves, ureters and bladder. A soft-tissue mass was present in the midline at the level of the second lumbar vertebra that caused an extrinsic defect on the stomach distal to the angulus. The psoas shadows were distinct. Barium examination of the colon showed it to fill readily without obstruction; the examination was unsatisfactory, but the above described mass seemed to be extrinsic to the colon. The cecum was freely movable and nontender. The mucosal pattern was normal.

A gastrointestinal series showed a normal esophagus. The stomach was deformed by pressure from an extrinsic mass beginning at the angulus on the greater curvature and filling the space between the angulus and the descending loop of the duodenum (Fig. 1). The mucosa over this large, smooth, round mass showed no ulceration. As soon as the barium entered the second portion of the duodenum, a large clump of barium was seen in the region of the mass that showed no mucosal pattern. The barium, however, did pass into the jejunum, and in the lateral projection this seemed to lie posteriorly, widening the duodenal curve. Films taken three hours after the meal showed a large mass of barium still in the region of the mass (Fig. 2). A 1-by-2-cm. area that was free of barium was present above the mass. This area was constant in size, shape and position.

On the third hospital day the patient had a fever of 103°F., with a subsequent fall to normal. She was given 4 mg. of Hykinone intramuscularly every day for three days and then three times a week. The pain was controlled by sedation. On the tenth hospital day the temperature rose to 102°F., and from then on ranged between 102 and 98.6°F. She was given 6 gm. of sulfadiazine daily, several transfusions of whole blood and intravenous fluids.

On the seventeenth hospital day an operation was performed.

DR. JACOB LERMAN: I saw this patient on rounds. Our first impression was that she probably had carcinoma of the transverse colon. After seeing the x-ray films we thought that it had ruptured, had formed a large abscess around the colon and had gradually involved the surrounding organs to explain this peculiar x-ray picture. We also considered hypernephroma, but after seeing the x-ray films we dismissed that diagnosis. Carcinoma of the gall bladder was likewise considered. Most of the service thought that it was carcinoma of the colon.

DR. MOORE: I should have mentioned that the single observation of a positive Graham test without stones does not prove anything one way or another. Since the dye was given by mouth, the pathology in this region could have impaired absorption.

DR. LINTON: Did the mass pulsate?

DR. BENJAMIN CASTLEMAN: No.

CLINICAL DIAGNOSIS

Abdominal tumor (? carcinoma of pancreas).

DR. MOORE'S DIAGNOSIS

Carcinoma of neck or body of pancreas?

Carcinoma of gall bladder, with erosion into duodenum?

ANATOMICAL DIAGNOSIS

Epidermoid carcinoma of gall bladder, with fistulous extension into duodenum and transverse colon.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At operation the surgeon found a huge mass in the right upper quadrant on the

undersurface of the liver and took a small piece. He was also able to scoop out several stones that apparently he got into the center of the bladder. The tissue proved to be an epidermoid carcinoma.

The patient died soon after operation and autopsy showed a mass that measured roughly 20 cm. diameter, which superiorly was firmly attached to the inferior surface of the right lobe of the liver inferiorly had pushed the transverse colon quite a bit. In dissecting the bile ducts we were able to find only the beginning of the cystic duct; the rest of the cystic duct and the gall bladder were replaced by the mass. In the center of it was a large amount of necrotic material, which was secondarily infected. The tumor had perforated into the second portion of the duodenum and also into the transverse colon in two places. The perforation into the duodenum at the time of autopsy measured $\frac{1}{2}$ cm. diameter, and those in the transverse colon measured about 1.5 cm. in diameter. Since the gall bladder had been replaced by the mass and because of the fact that the tumor was an epidermoid carcinoma the diagnosis of carcinoma of the gall bladder becomes fairly certain. There was no involvement of the pancreas.

DR. MOORE: If the tumor had invaded the duodenum on its medial wall it must have involved the pancreas.

DR. CASTLEMAN: It was not exactly medial; anteromedial is a better way of describing it. In the gross examination and in the sections the pancreatic parenchyma was not involved.

DR. ROBBINS: From the x-ray appearance the tumor had to involve the stomach.

DR. CASTLEMAN: Yes; it was adherent to both the stomach and the pancreas but had not invaded either.

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The diagnosis of infectious mononucleosis depends on evidence that is rather well defined. Usually the physical examination, blood studies and clinical course suggest the proper diagnosis, which may be confirmed by the sheep-cell agglutination reaction. If infectious mononucleosis is borne in mind in the differential diagnosis of fevers of unknown origin, there should be little difficulty in arriving at the correct diagnosis in most cases. It seems likely that the incidence of this disease, particularly among children and young adults, may be greater than is ordinarily supposed.

The diagnosis of undulant fever is often troublesome. Most cases present few significant physical findings. Often it is difficult to recover the etiologic agent from the blood stream, and positive serologic and skin tests are not necessarily indicative of active infection since both tests may be positive because of previous infection or because of continued use of milk from infected herds.

The authors point out that epidemiologic investigations of cases of undulant fever may be helpful in the diagnosis of this disease. For the most part it is acquired by ingestion of infected dairy products or by contact with animals. It was observed that when reported cases could not be traced either to raw milk or to infected animals, review of the clinical findings sometimes resulted in a change in diagnosis.

Although undulant fever is usually thought of as a rural disease, it may occur among persons living in urban areas in spite of local regulations that forbid the sale of raw milk. In such cases the urban residents usually acquire the disease by the ingestion of raw milk while traveling in regions remote from their homes. Hardy et al.,* in a study of 17 patients living in New York City who had been exposed to infection through the use of raw milk ingested during single out-of-town visits, reported incubation periods varying from one week to four months, the longer one tending to obscure the source of infection. Other urban residents may contract undulant fever as a result of occupational exposure. For example, direct contact with animals or animal carcasses by persons employed in packing

*Hardy, A. V., Frant, S., and Kroll, M. M. Incubation period in undulant fever. *Pub. Health Rep.* 53:796-803, 1938.

INFECTIOUS MONONUCLEOSIS VERSUS BRUCELLOSIS

An article published in this issue of the *Journal* indicates that the differential diagnosis of infectious mononucleosis and brucellosis may give rise to considerable confusion. The authors discovered 13 cases of infectious mononucleosis by performing the heterophile antibody reaction routinely on a series of one thousand consecutive samples of blood serum submitted by physicians to the State Bacteriological Laboratory for undulant-fever agglutination tests. In 11 of the cases, the physician had not suspected this disease.

houses or rendering plants is often the source of infection. For this reason a careful occupational history may be helpful in the diagnosis of this disease.

Not so many years ago, application of a simple rule of thumb, "Tuberculosis, typhoid fever and sepsis," was fairly adequate in the differential diagnosis of obscure fever. Because of the ever-dwindling incidence of acid-fast and typhoid infections, however, other causes of obscure fever are now becoming relatively more frequent. The State Department of Public Health announces the availability, on request by physicians, of the heterophile antibody reaction. This test should provide additional aid in the diagnosis of unexplained fevers.

PENICILLIN IN EXPERIMENTAL VIRAL AND RICKETTSIAL DISEASES

With few notable exceptions, the new chemotherapeutic agents have been ineffective in the treatment of viral and rickettsial diseases. The exceptions are lymphogranuloma venereum, trachoma and inclusion blenorrhea, which apparently respond favorably to most of the sulfonamide drugs that are now in general use. With the advent of penicillin, it is natural that the field of viral and rickettsial disease should be re-explored for the possibility that infection with some of these nonbacterial agents might prove susceptible to its action. Thus far, no really successful clinical trials in this field have been reported. A few recent studies suggest that penicillin in adequate doses is effective in reducing the mortality from experimental infection of animals with some of these agents.

Heilman and Herrell,^{1, 2} of the Mayo Clinic, have published studies on experimental ornithosis and psittacosis in mice. With both viruses, the authors noted a marked reduction in mortality among the penicillin-treated animals. The virus could always be recovered from the surviving animals long after treatment had been stopped. They suggest that penicillin inhibits the multiplication of virus until immunity has been established. The treatment apparently converted an acute and fatal infection into one that was chronic and relatively benign. The possibility that bacterial infections were present

to account for the differences was not adequately controlled. Furthermore, the results would have been somewhat more convincing had the authors controlled the series with similar sulfonamide-treated animals.

Experiments on the effect of penicillin on murine typhus in the yolk sac of developing chick embryos and in susceptible mice have been carried by Pinkerton and his associates.^{3, 4} These workers conclude that penicillin injected in three doses at intervals of forty-eight hours exerted a striking inhibitory effect on the multiplication of the rickettsias of murine typhus in the yolk sac of the fertilized hen's egg. In these experiments, penicillin was not injected until two or three days after the injection of the rickettsias in order to allow time for the organisms to gain entrance into the cells. Careful study was made of the cells in the yolk sacs of the penicillin-injected eggs, and with the exception of some heavily infected eggs, only a rare isolated organism was seen in such a position that it might have been thought to be intracellular. These observations suggest that the inhibition of rickettsial growth was brought about by penetration of the penicillin into the cells rather than by its direct effect on extracellular organisms in the process of passing from cell to cell.

In mice, Pinkerton and his associates showed that the administration of penicillin in relatively large but nontoxic doses after infection with the rickettsias of murine typhus resulted in a marked reduction in mortality, particularly when the initial infective dose was relatively small, approaching the minimum lethal dosage. They found no evidence of secondary bacterial infection in bacteriologic and histologic studies and thus felt justified in concluding that the greatly increased survival rate in the penicillin-treated mice was caused by the action of penicillin on the rickettsias. The penicillin was usually injected intraperitoneally, and in most of their experiments, there was a daily period of nine hours during which the concentration of the drug was probably not maintained at effective levels. They suggest that, since the human disease is caused by the growth of rickettsias in vascular endothelium, intravenous or intramuscular injection of penicillin should bring the drug into direct contact with the

containing the organisms and that, if sufficiently high concentrations of the drug can be established in the blood stream in the early stages of the disease, it is reasonable to expect a beneficial therapeutic effect. They believe that their results justify a thorough clinical trial of penicillin in human typhus fever. They suggest that treatment in the early stages of the disease is necessary and that the dosage should be increased over that ordinarily used in bacterial infections.

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MASSACHUSETTS MEDICAL SOCIETY

EATHS

AUSTIN—James C. Austin, M.D., of Spencer, died July 10. He was in his sixty-ninth year.

Dr. Austin received his degree from Baltimore Medical College in 1896. He had been a practicing physician in Spencer for forty years and was widely known throughout Worcester County. He was chairman of the Board of Health for twenty-five years and served as school physician for many years. He was a past president of the Worcester District Medical Society and a member of the American Medical Association and the Brookfield Medical Society.

His wife, three daughters, a brother and a sister survive.

CUMMINGS—John J. Cummings, M.D., of Worcester, died July 9. He was in his seventy-fifth year.

Dr. Cummings received his degree from Columbia University College of Physicians and Surgeons in 1899. He had been a practicing physician in Worcester and a member of the St. Vincent Hospital staff for more than forty years. For the past fifteen years he had been senior member of the hospital obstetric staff. He was a member of the American Medical Association.

His widow, two sons and two brothers survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

LABORATORY TEST FOR INFECTIOUS MONONUCLEOSIS

The Bacteriological Laboratory at the State House is now prepared to perform tests for heterophile antibody (sheep-cell agglutination) as a means of detecting cases of infectious mononucleosis. Although infectious mononucleosis is not reportable, its infectious character has been recognized for some time.

In a recent study carried on by this department, the results of which appear elsewhere in this issue of the *Journal*, it has been shown that a certain

proportion of blood serums submitted by physicians for the undulant-fever agglutination test gave positive tests for heterophile antibody. Because of the similarity in the clinical manifestations of undulant fever and infectious mononucleosis, one may easily be confused with the other. It is thought that the availability of this test will assist physicians further in diagnosing fevers of undetermined origin.

Physicians requesting this test should submit 5 to 10 cc. of whole blood or serum in a dry, preferably sterile, test tube. The undulant fever outfit issued by this department is adequate for the purpose.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1944

RÉSUMÉ

DISEASES	JUNE 1944	JUNE 1943	SEVEN YEAR MEDIAN
Anterior poliomyelitis	1	2	2
Chancroid	4	*	*
Chicken pox	1748	1011	1170
Diphtheria	7	7	7
Dog bite	1221	1465	1410
Dysentery, bacillary	2	1	2
German measles	200	3682	153
Gonorrhea	442	420	355
Lymphogranuloma venereum	4	*	*
Measles	3019	5320	3918
Meningitis, meningococcal	28	74	13
Meningitis, Pfeiffer bacillus	—	2	1
Meningitis, pneumococcal	3	4	†
Meningitis, staphylococcal	—	—	†
Meningitis, streptococcal	—	—	†
Meningitis, other forms	1	2	†
Meningitis, undetermined	8	8	†
Mumps	966	611	641
Pneumonia, lobar	215	200	230
Salmonella infections	13	4	6
Scarlet fever	904	1442	723
Syphilis	458	499	417
Tuberculosis, pulmonary	324	308	312
Tuberculosis, other forms	19	23	24
Typhoid fever	2	3	7
Undulant fever	5	6	4
Whooping cough	248	465	379

*Made reportable in December, 1943

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941

COMMENT

Anterior poliomyelitis, fortunately, continued at a low level. The incidence for the past six months is lower than that for the corresponding months in 1943.

Chicken pox showed the usual seasonal decline but was still the highest on record for the month of June.

Diphtheria showed a marked drop after nine months of unusually high prevalence.

Meningococcal meningitis showed a definite decline from March through June, but the prevalence was still above that of 1942. It appears that the peak was reached during the fall and winter and that there will be a gradual decline to interepidemic levels.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from Medford, 1, total, 1.

Anterior poliomyelitis was reported from Boston, 1, total, 1.

Anthrax was reported from Lowell, 1, total, 1.

Diphtheria was reported from Auburn, 1, Boston, 1, Lawrence, 1; Medford, 2; Needham, 1, Somerville, 1, total, 7.

Dysentery, amebic, was reported from Cushing General Hospital, 1; total, 1.

Dysentery, bacillary, was reported from Worcester, 2, total, 2.

Encephalitis, infectious, was reported from Fall River, 1, Needham, 1, New Bedford, 1; total, 3.

Malaria was reported from Boston, 2, Camp Edwards, 11, Cushing General Hospital, 20, Fall River, 2, Fort Banks, 5, Fort Devens, 13; New Bedford, 1, Salem, 2, Somerville, 1, Woburn, 1, Worcester, 1, total, 59.

Meningitis, meningococcal, was reported from: Arlington, 1; Boston, 8; Braintree, 1; Chelsea, 1; Chicopee, 1; Dennis, 1; Fall River, 1; Fitchburg, 1; Fort Devens, 1; Lawrence, 1; Ludlow, 1; Medway, 1; Nahant, 1; Newton, 1; Oxford, 1; Revere, 1; Springfield, 2; Stoughton, 1; Waltham, 1; Wrentham, 1; total, 28.

Meningitis, pneumococcal, was reported from: Boston, 2; Framingham, 1; total, 3.

Meningitis, other forms, was reported from: Boston, 1; total, 1.

Meningitis, undetermined, was reported from: Boston, 3; Quincy, 2; Winchester, 1; Worcester, 1; Wrentham, 1; total, 8.

Salmonella infections were reported from: Arlington, 1; Boston, 1; Boylston, 1; Cambridge, 1; Everett, 1; Hopedale, 1; Ludlow, 1; Malden, 1; Melrose, 1; Milton, 1; Revere, 1; Salem, 1; Worcester, 1; total, 13.

Septic sore throat was reported from: Arlington, 1; Belmont, 1; Boston, 7; Holyoke, 1; Merrimac, 2; Topsfield, 1; total, 13.

Tetanus was reported from: Dartmouth, 1; Medford, 1; total, 2.

Trachoma was reported from: Beverly, 1; total, 1.

Trichinosis was reported from: Lowell, 2; total, 2.

Typhoid fever was reported from: Boston, 1; Gardner, 1; total, 2.

Undulant fever was reported from: Billerica, 1; Concord, 1; Holyoke, 1; Saugus, 1; Williamstown, 1; total, 5.

MISCELLANY

PULMONARY TUBERCULOSIS ASSOCIATED WITH CONGENITAL HEART DISEASE

When a patient with congenital heart disease acquires tuberculosis it is a serious mishap. The medical adviser must then make the choice between conservative treatment of the tuberculosis and some form of collapse therapy with the attendant risk of burdening the already embarrassed circulatory systems still further. A recent study of a number of cases (Auerbach, O., and Stemmerman, M. G. Development of pulmonary tuberculosis in congenital heart disease. *Am. J. M. Sc.* 207:219-230, 1944) suggests that prompt and active therapy directed at the tuberculosis offers the best chance of preserving the already short life span of these individuals.

* * *

It is commonly accepted that patients suffering from congenital heart disease are prone to develop and later to succumb to pulmonary tuberculosis. Of all patients with congenital heart anomalies it is those with pulmonary stenosis who seem most likely to develop tuberculosis. Whether it occurs more frequently in this group than among a comparable number with normal hearts cannot be stated positively without detailed statistical analyses. Case reports seem to show that tuberculosis is no greater menace in patients with pulmonary stenosis than is their cardiac defect.

It is true, however, that many persons born with this anomaly die before they have relatively much opportunity to develop tuberculosis, many of them being so incapacitated that they are protected from infectious contacts. If predisposition does actually exist it must arise primarily in the faulty oxygen and blood exchange characteristic of these cases.

This study concerns the frequency of congenital heart conditions in a tuberculosis institution, the course of the pulmonary disease and the efficacy and advisability of collapse therapy in the face of the cardiac handicap.

In the course of 1545 necropsy examinations of tuberculous persons, 7 cases of congenital heart disease were discovered, an incidence of 0.4 per cent. This incidence may be higher than in most other tuberculosis institutions owing to the fact that one out of eight beds in this hospital is allotted to peditrics. It is lower than that observed in institutions devoted entirely to the treatment of children.

The diagnosis made from the symptoms and physical examination of 6 additional patients coincided unusually well

with the defects found in the 7 cases that came to autopsies. They exemplify the grouping of cardiac anomalies known as the "tetralogy of Fallot." A picture of this condition is represented by this composite case report: The patient, a white youth in his lower teens. The history records symptoms from birth or shortly thereafter, and the diagnosis of congenital heart disease was made early. At that time he was placed on restricted activity and followed in a hospital out-patient department. He has had no evidence of congestive failure and has led a fairly normal life until the onset of the pulmonary disease. Examinations show a young appearing underdeveloped child not, as a rule, dyspnoeic but with cyanosis and clubbing of the fingers and toes. The heart is enlarged in all dimensions, with a loud, harsh, systolic murmur at the base, usually associated with a systolic thrill. The lung findings are dependent on the pulmonary pathology. Laboratory tests indicate a well-marked polycythemia, and there are tubercle bacilli demonstrable in the sputum. Roentgenography and fluoroscopic examination demonstrate enlargement of both ventricles, frequently more marked in the right, and a prominent pulmonary conus. The venous pressure is within normal limits, and the blood pressure tends to be normal or slightly decreased. In the electrocardiogram is found right-axis deviation with tall P waves, these often being notched. The pulmonary disease has not influenced the findings typical of the combined heart lesions making up the cyanotic group.

The onset of pulmonary disease in these cases was similar to that of patients without congenital heart disease. Some or all of the usual symptoms of tuberculosis were present in all cases. No difficulty was experienced in differentiating the congenital heart disease and pulmonary tuberculosis since the congenital anomaly was diagnosed in 4 cases prior to the onset of the tuberculosis. The disease was moderately or far advanced on admission to the hospital in all but 1 case. The course of the disease and the lesions at autopsy were similar to those observed in patients without the cardiac hazard. The duration of life depended on the extent of the disease on admission and the effectiveness of collapse therapy when that was used. The longest duration in the series of 13 cases was six years, the shortest course was seven months. The average duration of life from the onset of the pulmonary infection to fatal termination was one to two years.

As the lesions and other factors of the pulmonary infection are the same whether or not the patient has congenital heart disease and as the cause of death depends on the pulmonary rather than the cardiac status, it is the lung rather than the heart that should be the local point of therapy. When best rest fails to arrest the progression of the tuberculous infection or cannot accomplish cavity closure it must be supplemented by collapse therapy in spite of the cardiac pathology. When this procedure is adopted late in the course of the disease the possibility of arresting the tuberculosis is slight. The life expectancy of these patients even without the pulmonary complication is short. Nevertheless, therapeutic measures even hazardous ones, seem justifiable if they will prevent the patient from succumbing even more prematurely to tuberculosis.

In the group of cases here reported pneumothorax was instituted in 5 cases. In 1 case only was an effective pneumothorax established. In no case did collapse therapy increase the cardiac symptoms or lead to congestive heart failure.

It is recommended that congenital heart disease should not be considered a contraindication to thoracoplasty at least in order not to deprive these patients of the few years of life expectancy due them, immediate operation may be more advantageous than a preliminary, often disappointing, trial of pneumothorax. — Reprinted from *Tuberculosis Abstracts* (August, 1944).

NOTE

Dr. H. Houston Merritt, associate professor of neurology, Harvard Medical School, and visiting neurologist, Boston City Hospital, has been recently appointed professor of clinical neurology, Columbia University College of Physicians and Surgeons, and chief of the Division of Neuro-psychiatry, Montefiore Hospital, New York City.

BOOK REVIEWS

Mechanism: A physiologic interpretation of causalgia and its related states. By W. K. Livingston, M.D. 8°, cloth, pp., with 26 illustrations and 1 table. New York: The Millan Company, 1943. \$3.75.

Dr. Livingston, a neurosurgeon, has long been interested in the clinical aspects of pain, and this book is a personal record of his investigations of the last few years. He points out what we know about the mechanism of pain and indicates further researches that might be made with profit. The chapters cover the anatomy of pain pathways, the pathology and physiology of pain, the various clinical syndromes and the author's interpretations of the pain phenomenon.

Dr. Livingston draws no final conclusion, since the subject is too complicated, and many questions are still unanswered. He has, nevertheless, certain convictions. One at the concept of specificity in the narrow sense in which it is sometimes used to identify sensory experiences with particular end-organs and nerve fibers has led away from a perspective. He also thinks that it is a mistake to assume that certain pain syndromes must represent an obsession of the psychiatrist's origin. He does not discredit the results of peripheral sympathectomy and novocain injections, but on the ground that their mode of action is obscure. He believes, finally, that chronic irritations of sensory nerves initiate clinical states that are characterized by pain spreading disturbances of function in both somatic and visceral structures. If such disturbances continue, he thinks they are profound, and perhaps unalterable, organic changes may take place in the affected part. The aim of therapy should be to break up this vicious cycle, even if it requires the permanent removal of an anatomic pathway. In many cases, however, simple removal of the trigger point is sufficient to establish relief.

The book in general is a thoughtful summary of a controversial subject and as such is a distinct addition to medical literature.

Coroners Anonymous: The story of laboratory medicine. By William McKee German, M.D. With an introduction by J. de Kruijff. 8°, cloth, 300 pp. New York: Duell, Sloan Pearce, 1941. \$2.75.

The doctors referred to in the title are the pathologists, the author being a distinguished example of that group of scientists. This book is written in an interesting but truly instructive manner for the public and explains the work of the pathologist in a general hospital, as well as including certain details regarding bacteriology and tissue diagnosis from relative specimens, the importance of the autopsy to both the medical profession and the public, and a plea for recognition of the value of the pathologist's position in hospitals. There is an excellent chapter on the coroner's system. It is surprising to learn that in forty-four of the states and in the District of Columbia, sudden, unexplained deaths are investigated by a coroner, and in only six of these states is the coroner required to be a licensed physician. Thus, why people die is a large part of the country is investigated by undertakers, furniture dealers who sell caskets and former politicians with good political connections. Massachusetts, ahead of other states, gave up the coroner system as early as 1877, but it took nearly fifty years for some of her neighbors to follow suit. In spite of state laws, certain cities, particularly New York and San Francisco, have excellently trained medical examiners, who perform the autopsies.

Finally, the author discusses various diseases that, at some time in the history of the country, were important to the pathologist but now are practically extinct, such as chlorosis, scrofula and most types of lead poisoning. There is much of interest to any physician in this well-written book.

Clinical Diagnosis by Laboratory Examinations. By John A. Limer, M.D., Dr.P.H., Sc.D., LL.D., LL.D. 8°, cloth, 59 pp., with 75 illustrations. New York: D. Appleton-Century Company, 1943. \$8.00.

The size of this volume attests to the importance of the laboratory as an integral part of diagnosis. The author offers apologies for those who would circumvent careful clinical study by resorting to numerous laboratory procedures in

the hope of reaching a diagnosis. It has become almost platitudinous to stress the importance of the sequence of bedside study supplemented by any and all necessary laboratory tests. Clinical acumen still has its place.

This book is divided into three portions: the clinical interpretation of laboratory examinations; the practical application of laboratory examinations in clinical diagnosis; and the technic of laboratory examinations. Thus both the laboratory procedures and the tests of visceral functions are discussed, supplemented by numerous tables, which add greatly to the value of the book.

Attention may be called to certain minor omissions and corrections. The frequency with which laboratories report some results in milliequivalents calls for some elucidation. The determination of the ketosteroids in the differentiation of Simmonds's disease and anorexia nervosa is not mentioned. The role of perforated eardrums in yielding faulty basal metabolic readings should be noted. In discussing platelet counting the direct method is entirely omitted, and Dr. Olef's name is misspelled.

On the whole, this is a book that richly deserves a handy place not on the shelf but on the laboratory table or desk.

Burma Surgeon. By Gordon S. Seagrave, M.D. 8°, cloth, 295 pp., with 22 illustrations and frontispiece. New York: W. W. Norton & Company, Incorporated, 1943. \$5.00.

This book, one of the best sellers of 1943, hardly needs any introduction to the medical profession. It is an outstanding book of the war by a man whose personality is stamped on every page.

To a missionary doctor in Burma came an opportunity as the result of the war to do a job far greater than anything he had anticipated when he went to his station. Fortunately for the world and for the British and American troops involved, Dr. Seagrave proved to be a man of exceptional quality. He not only had excellent surgical judgment but also knew how to administer an organization and train its personnel. He took the native women and taught them to be first-class nurses. When General Stilwell and his army had to retreat, Dr. Seagrave became one of the outstanding members of that memorable march.

This book, if not already read by every member of the profession, should not be missed.

Exploring the Dangerous Trades: The autobiography of Alice Hamilton, M.D. 8°, cloth, 433 pp., with 7 illustrations and frontispiece. Boston: Little, Brown and Company, 1943. \$3.00.

Dr. Hamilton is one of the great pioneer physicians of this country, and her autobiography is an unusually striking contribution. Her early life during the last decade of the nineteenth century was spent in Chicago, where she was associated with the pioneer social experiment at Hull House. There she came in contact with poverty, disease and particularly industrial accidents, and from this background, plus an adequate knowledge of pathology, a subject that she taught for many years at Northwestern University, Dr. Hamilton became an authority on diseases associated with workmen and working conditions. She made an extensive survey of Illinois, pioneering and exploring an almost unknown field. Later, this was extended into a federal survey of "dangerous trades," with final extension to Europe. Ultimately, she became a member of the staff of the Harvard Medical School, where she continued her work for many years. In 1935, having become a professor emeritus at Harvard, she retired to Connecticut, where she lives quietly in the country, occupied with her writing.

The book is a delightfully written, simple, straightforward story of a woman who has made distinct additions to the knowledge of industrial diseases. All through her account one feels that she is an extremely human character, with a personality that must have appealed to a great many people. She writes pleasantly about her associates and neighbors, and the book is of unusual interest, as well as a stimulating experience.

The Kenny Concept of Infantile Paralysis and Its Treatment. By John F. Pohl, M.D. In collaboration with Sister Elizabeth Kenny. With a foreword by Frank R. Ober, M.D. 8°, cloth, 386 pp., with 100 illustrations. Minneapolis: Bruce Publishing Company, 1943. \$5.00.

This book has the official sanction of Sister Kenny, since she collaborated with the author in writing it. It is, therefore, an up-to-date discussion of the technic advocated by Sister Kenny, with a plan of the relief of pain and muscle spasm in poliomyelitis by the early and continued use of hot packs, as well as the procedure designed to re-educate the neuromuscular system. The application of moist heat is not a new one, since it was advocated as early as 1916 by Lovett and his co-workers. Sister Kenny's contribution in part has been the application of this form of treatment early in the course of the disease — as soon as the diagnosis has been made.

The first part of the book deals with this period of the disease and is fully illustrated with photographs and diagrams, showing the details of the Kenny technic. The second part covers the convalescent stage of the disease and is also fully illustrated. Finally, the third section is concerned with the treatment of patients in the chronic stage.

This text, with its many illustrations, is fundamental for an understanding of the Kenny concept of the treatment of infantile paralysis and should be in the hands of everyone concerned with the care of patients with this disease.

A History of Tufts College Medical School: Prepared for its semi-centennial 1893-1943. By Benjamin Spector, M.D. 8°, cloth, 414 pp., with 49 illustrations. Boston: Tufts College Medical School Alumni Association, 1943. \$5.00.

As a medical historian, the author is to be complimented for his singularly lucid and succinct semicentennial story of the Tufts College Medical School. Beginning with the removal of the restriction in the original Tufts College charter, which prevented the conferral of medical degrees, he describes from original sources the establishment of the school on October 4, 1893, and sketches by decades its course to the present time. Many of these documents are reproduced in facsimile. There are illustrations of the several buildings of the school, and many reproductions of graduation and other programs. Particularly valuable are the sketches of the original seven founders and the biographies of other distinguished Boston physicians of the epoch. This well-documented volume constitutes an enduring and worthy record of the first half century of one of the leading New England schools of medicine.

Kinetic Bandaging including Splints and Protective Dressings: The kinetic method of visual teaching. By Seymour W. Meyer, M.S., M.D. 8°, cloth, 310 pp., with 540 illustrations. Philadelphia: F. A. Davis Company, 1943. \$3.50.

The present is a good time to emphasize the importance of knowing how to apply a bandage, particularly since too little attention in recent years has been paid to this art. The primary purpose of bandaging, when employed as a final step in a surgical operation, is to secure a dressing in contact with the operative incision, but there are other quite as important services that a bandage may provide. This book, through its well-planned illustrations, could make a skilled bandager out of the veriest tyro. The methods of using adhesive plaster and the utility of the triangular bandage are equally well outlined.

The book should find a place in the hands of everyone who needs to be familiar with the application of surgical dressings. The success of an operation in some cases and the comfort of the patient in most cases are largely influenced by the skill with which a bandage is applied.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Lectures on Peace and War Orthopedic Surgery. Selected from the instructional courses presented at the eleventh annual assembly of the American Academy of Orthopaedic Surgeons, Chicago, January 17, 18, 19, 20 and 21, 1943. Edited by James E. M. Thomson, M.D., chairman of the instruc-

tional section. 4°, cloth, 322 pp., illustrated. Ann Arbor, Michigan: Edward Brothers, Incorporated, 1943. \$4.00.

This volume forms the transactions of the instructional section of the 1943 meeting of the American Academy of Orthopedic Surgeons. The volume contains sixty-five papers by military and civil medical authorities and is illustrated with half-tone reproductions of x-ray films and drawings which are reproduced by photolithography.

Physiology of the Nervous System. By John Farquhar F.C.M.A., D.Phil., D.Sc. (Oxon.), S.B., M.D. (Fav.). 8th edition, revised and reset. 8°, cloth, 614 pp., with 112 illustrations. London: Oxford University Press, 1943. \$9.00.

The reviewer believed that the first edition of this work was an outstanding contribution to the subject; his opinion is reinforced by the appearance of the second edition, thoroughly revised and brought up to date. The book can be highly recommended to medical students, physicians, workers in laboratories and libraries. It is, indeed, a fundamental text that should find a place on the shelf of all medical libraries, both public and private.

The Arthropathies; A handbook of roentgen diagnosis. By Alfred A. de Lormier, M.A., M.D., colonel, Medical Corps, United States Army, and commandant, Army School of Roentgenology, Memphis, Tennessee. 8°, cloth, 319 pp., with 678 illustrations. Chicago: The Year Book Publishers, Incorporated, 1943. \$5.50.

This handbook is a compilation of lectures presented by the officers of the Army Medical School in Washington and the Army School of Roentgenology in Memphis. The material is presented in the form followed in the teaching, which is largely graphic. There are a large number of roentgen plates.

Human Constitution in Clinical Medicine. By George Drap M.D., associate professor of clinical medicine, College of Physicians and Surgeons, Columbia University, and associate attending physician, Presbyterian Hospital, New York City; C. W. Dupertuis, Ph.D., physical anthropologist, Constitution Clinic, Presbyterian Hospital, New York City; and J. L. Caughey, Jr., M.D., Med.Sc.D., associate professor of medicine, College of Physicians and Surgeons, Columbia University, and assistant physician, Presbyterian Hospital, New York City. 8°, cloth, 273 pp., with 29 illustrations and 30 tables. New York: Paul B. Hoeber, Incorporated, 1943. \$4.00.

This manual is designed for the use of medical students and is written from the clinical point of view, with the objective of showing that there is an essential relation between each patient and the disease that at any moment he or she may suffer.

Psychosomatic Diagnosis. By Flanders Dunbar, M.D., M.Sc.D., Ph.D., member, Department of Medicine and Department of Psychiatry, Columbia University. With a foreword by Leonard G. Rowntree, M.D., colonel, Medical Reserve Corps, United States Army, and chief, Medical Division, Bureau of Selective Service of the War Manpower Commission, Washington, D. C. 8°, cloth, 741 pp., with charts and 12 tables. New York: Paul B. Hoeber, Incorporated, 1943. \$7.50.

This new treatise in a new field of medicine has been written for the use of the general practitioner and also serve as a guide in teaching. Emphasis has been placed on the fundamental importance of a complete case history after which special chapters are devoted to fractures, cardiovascular disease, rheumatic disease, cardiac arrhythmia and diabetes. A large number of clinical case histories are included in the text; also there is appended a large bibliography.

The Philosophy of Marsilio Ficino. By Paul O. Kristeller, associate in philosophy, Columbia University. Translated into English by Virginia Conant. 8°, cloth, 441 pp. New York: Columbia University Press, 1943. \$4.50.

This book was originally written in German in 1937, and the translation is the first study in English of Ficino, who was a physician and leader of the Platonic Academy in Florence.

(Notices on page xvii)

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TULAREMIA IN NEW ENGLAND

A Review of Eighteen Cases, with the Report of Two Additional Cases

FRANCIS D. MOORE, M.D.,* CARL S. SAWYER, M.D.,† AND S. GILBERT BLOUNT, JR., M.D.‡

BOSTON, MASSACHUSETTS, AND PROVIDENCE, RHODE ISLAND

THE term "tularemia" has been applied to a wide variety of illnesses due to human infection by *Pasteurella tularensis*. The most frequently occurring clinical picture is that of an open ulceration with regional lymphadenopathy and evidence of a severe systemic infection that appears to be out of proportion to the local lesion. This ulceroglandular form of the disease may be accompanied by mucocutaneous involvement, rash or enlargement of the spleen. The infection may also produce a form of the disease in which the systemic factors entirely outweigh the local lesion, in which event the typhoid form of the disease is found. The organism responsible for this infection is apparently endemic in a fairly widespread animal reservoir and is transmitted from animals to human beings either by an insect bite, by direct handling or by ingestion of infected animal material.

The ulceroglandular form of tularemia so closely resembles various trivial nonspecific peripheral infections and infected lacerations that it is often overlooked. Furthermore, the local lesion may be so minor as to be completely overshadowed by the systemic manifestations, leading to a mistaken diagnosis of blood-stream infection with gram-negative bacilli such as the typhoid bacillus or a febrile illness such as brucellosis, rheumatic fever or subacute bacterial endocarditis. It is therefore necessary to stress the importance of this disease in differential diagnosis and the need of an exhaustive search for a possible local lesion in the presence of fever of unknown origin. Because of these facts, as well as the appearance of 2 recent cases in New England, it has seemed worth while to review the history of tularemia in New England, bringing the literature on all the available cases up to date.

New England appears to have been the last region of the United States to remain free of infection with *Past. tularensis*. By 1932, tularemia

had appeared in all the states of the Union except Maine, Vermont and Connecticut¹; New England could claim the fewest cases of any sizable region in the country and contained the only three case-free states. Since that time, cases have appeared in New England at the rate of approximately 2 a year, and at the present time it is possible to bring together a total of 20 cases. Vermont remains as the only state apparently free of the disease.

Whether this phenomenon is due to an increasing incidence of tularemia in the region or merely to increasing recognition and bacteriologic confirmation is an academic question that cannot be answered on the basis of the material at hand. Although the disease was first described in animals, in California, by McCoy and Chapin in 1911,^{2,3} there is no way of knowing how widespread the animal reservoir was at that time. In 1919 Francis⁴ described the human disease as occurring in Utah, approximately five hundred miles from Tulare County in central California, where McCoy and Chapin had discovered the micro-organism seven years before. This geographical trend, however, is difficult to evaluate in the light of the fact that by 1938 over 1000 cases had been reported⁵ from Russia, apparently contracted from the skinning of water rats, and many other cases had been found in Japan, Norway, Canada, Sweden and Austria. By these data one is forced to the conclusion that although American in origin, scientifically speaking, the disease is of world-wide distribution.

In the light of these facts it is interesting that one region in America should apparently stay free of tularemia until 1929. Furthermore, the grouping of the New England cases indicates that factors of importation, either of rabbits or of infected human beings, seem still to be operative in the spread of the disease. This corroborates the impression that tularemia is still a relatively new disease in New England, not only to human beings but also to animals.

These factors of importation concern firstly 3 patients in the Boston area, one who contracted the

*Assistant in surgery, Massachusetts General Hospital, and instructor in surgery, Harvard Medical School, Boston

†Graduate assistant in dermatology, Massachusetts General Hospital, Boston

‡Intern, Medical Service, Rhode Island Hospital, Providence, Rhode Island

disease in Colorado and then came to Boston, a second who contracted it from tick bites while in Georgia and a third who contracted it from a rabbit shot in Illinois and shipped here. Furthermore, in 1936, cottontail rabbits were imported from the West and released near Falmouth, Massachusetts, and within two years 3 cases had been reported from that district. A fourth case occurred in the region of Falmouth in 1943. This makes a total of 7 cases in New England — nearly a third of the entire series — directly traceable to importation of infected animals or contracted elsewhere. It is impossible to say to what extent these importations have influenced the further spread of the disease in New England, but the fact that 4 more cases have occurred within seventy miles of the Falmouth area is suggestive.

CHRONOLOGICAL REVIEW OF NEW ENGLAND CASES

The first case to appear in New England was reported from Massachusetts by Withington.⁶ The patient contracted the ulceroglandular type of disease from tick bites while visiting on an island off the coast of Georgia in 1929. He had a septic abrasion on the scrotum, with an enlarged inguinal node that subsequently suppurated, and x-ray evidence of a slight pneumonitis on the left side. Widal and Wassermann reactions were negative, but the serum agglutinated *Past. tularensis* in a dilution of 1:1280 and *Brucella abortus* in a dilution of 1:160 (partial agglutination in a dilution of 1:320). Randall⁷ in 1929 reported a case in Rhode Island in which a man contracted tularemia after handling three dead rabbits. A cat that ate one of the rabbits also contracted the disease and died. Agglutination of the patient's serum against *Past. tularensis* was positive. The second case to appear in Massachusetts⁸ occurred in Boston in 1929. The patient evidently caught the disease from a cold-storage rabbit that had been frozen for thirty days and imported from Illinois. The patient had ulceroglandular tularemia with an urticarial eruption, and serum agglutination against *Past. tularensis* was positive in a dilution of 1:640.

Badger⁹ and Eckstein¹⁰ both referred to 2 cases, one occurring in New Hampshire in 1931 after the handling of rabbits and the other in Maine in 1933 after the skinning of a fox. Further details on these cases have not been found elsewhere in the literature, but the second one has been confirmed by the Maine Department of Health and Welfare.¹¹ The disease in this case was of the ulceroglandular form and was fatal. It was proved by autopsy, culture and agglutination.

In 1934,¹² a man contracted the ulceroglandular form of tularemia from the ingestion of a rabbit that he had killed on a ranch in Colorado. He returned to Boston after his symptoms had appeared and was hospitalized. Serum agglutination

was positive in dilutions up to 1:1280, and a test with the Foshay tularemia suspension was positive.

In 1935 and 1936, 3 cases were reported to the New Hampshire Department of Health.¹³ All three were clinically stated to be tularemia and accepted as such by the state authorities, but the detailed bacteriologic report are not available.

In 1937,⁹ a ten-year-old girl developed a typhoidal type of tularemia in Falmouth, without skin lesions or adenopathy, presumably from the saliva of her dog, which became ill three days later. Specific agglutination was positive in dilutions 1:1280. The dog serum was positive in dilution up to 1:40. This case appeared three months after Western cottontail rabbits had been released in the neighborhood of Falmouth. In the same district, one year later, another child developed ulceroglandular tularemia after being bitten by a tick. The bite was in the scalp and was accompanied by enlarged postaural nodes. Serum agglutination tests were not done. A Roxbury resident visiting Cape Cod in July, 1939, was bitten on the thigh by a tick, subsequently developing ulceroglandular tularemia with pneumonic symptoms.¹⁴ This patient, unlike the others, had severe systemic disease and serum agglutination tests were positive in dilutions up to 1:1280.

Gibbons, Lamoureux and Arkless¹⁵ described a case in Connecticut that occurred in December 1940. After killing and dressing three rabbits the patient developed tularemia with a finger ulcer, chills, fever and adenopathy, which subsided in three days. A relapse eleven days later with severe systemic disease proved fatal. Agglutination tests were positive in dilutions of 1:640.

In 1941, a man in Lawrence, Massachusetts, complained of an abrasion on his finger that subsequently became necrotic. The diagnosis of tularemia was established by history of exposure to rabbits that he had shot and dressed, as well as by the findings of adenopathy, chills, fever and a specific agglutination test in serum diluted to 1:640.¹²

A second case was reported from Rhode Island by Eckstein¹⁰ in 1941. The patient had the ulceroglandular form of the disease, contracted after dressing a rabbit that he had shot. The primary lesion appeared in a puncture wound of the hand sustained two days before. Specific agglutination was positive in serum dilutions up to 1:2560. This patient received sulfanilamide therapy.

Two other cases were reported from Connecticut in 1941. The first of these¹⁶ occurred in Columbia only ten miles from Colchester, where the previous Connecticut case had occurred.¹⁵ This was a fatal case of ulceroglandular tularemia, with pneumonic manifestations, contracted from a cat bite. The second was a case of ulceroglandular tularemia from handling rabbits,¹⁷ it occurred in Stamford. Agglutination tests were positive in a titer of 1:80.

The most recent New England case to appear prior to the 2 reported below was a fourth case from Falmouth district,¹² following a tick bite. The patient developed right-sided pneumonia without evidence of a primary lesion or adenopathy. Specific serum agglutination tests were positive.

REPORT OF CASES

CASE 1. The patient (M. G. H. Unit 405941) was a 52-year-old inhabitant of Waltham. He was admitted to the Emergency Ward on June 8, 1943, and stated that 3 weeks prior, while working in his garden, he had been bitten over the upper sternum by a small insect. He had not noticed the bite until he went into the house and looked in a mirror. He did not identify the insect, but when he removed and shed it, it appeared to be distended with blood and to have a hard shell.

For 3 days nothing further was noted about the incident. The end of that time the patient began to notice occasional chilly sensations, fever and considerable muscular weakness. Following a week of such symptoms, not severe enough to incapacitate him, he noticed soreness in the left axilla and a small papule at the site of the bite, which broke down and formed an ulcer that gradually increased in size. He poulticed the lesion and called in his physician, who gave him sulfadiazine totaling 3 gm. a day for 10 days. Since the fever and malaise persisted, as well as the ulcer and the sore in the left axilla, he was referred to the hospital.

On entry to the Emergency Ward the patient had a temperature by mouth of 101.8°F. and a white-cell count of 14,400. The urine was negative. The ulcer over the manubrium was 1.5 cm. in diameter, with a 3-cm. zone of erythema surrounding it. It was not tender and there was no undermining or penetration, but the edge was indurated. Little exudate was present, it was not granulating, and there was no evidence of undrained pus. A firm, tender, freely movable lymph node the size of a walnut was present in the left axilla. The patient had had no contacts with rabbits, ground squirrels or other rodents and the only small animals he had seen around his garden were chipmunks.* He did not remember seeing any that appeared ill, and no dead ones had been seen to his knowledge.

Tularemia was suggested as a tentative diagnosis, and the patient was admitted to the hospital. Primary syphilis, staphylococcus-streptococcus infection, anthrax, sporotrichosis and other mycotic infections were also considered. A blood culture yielded no growth, and serum agglutination tests against *Past. tularensis* done on admission were negative in all dilutions. Cultures from the ulcer, taken in the usual aerobic and anaerobic media, showed a coagulase-negative hemolytic *Staphylococcus albus*, diphtheroids and aerobic spore-formers. In addition, some yeasts were found that were cultured and studied for virulence by mouse injection, with negative results. Dark-field examination of the material from the ulcer for *Treponema pallidum* was negative. His blood serum gave a positive Hinton and a negative Wassermann reaction on two occasions. A Hinton test the day before discharge was negative. Agglutination tests for typhoid and paratyphoid fever were negative. Stool and urine cultures were negative.

The clinical course was one of continued swinging fever, with a high as 103.6°F., for the first 10 days in the hospital. The patient had few symptoms other than malaise. The white-cell count fell to 6000 by June 22 and he consistently showed a high monocyte percentage. He developed a node in the left axilla on June 11, and for 3 days thereafter he had generalized lymphadenopathy, the nodes being almond-sized, nontender and freely movable. There was no rash.

On June 21, to obtain material for histologic study to clarify the diagnosis, the ulcer was excised under Pentothal sodium anesthesia and the wound was closed with silk. The operative site healed cleanly, and the temperature immediately became normal and remained so until discharged 7 days later. The palpable nodes disappeared in 4 days.

*It is of interest in this connection that Zinsler¹³ states that chipmunks are among the more susceptible group of animals to infection with *Past. tularensis*. Welch and Jakmauh¹⁴ point out that the chipmunk is also one of the common hosts in this region for the wood tick *Dermacentor variabilis*.

The pathological report from the excised lesion was "acute and chronic inflammation," with no changes characteristic of either syphilis or other specific granulomas. Blood serum taken for heterophile agglutination on the same day as the operation was negative.

A repeated agglutination test for *Past. tularensis* showed the following results: serum diluted 1:20, +++; 1:40, +++; 1:80, ++; 1:160, ++; 1:320, ++. This positive agglutination, in the presence of a clinical picture compatible with the disease, established the diagnosis of the ulceroglandular form of tularemia. The fact that the earlier agglutination test was negative was attributed to its being taken too early, although the patient was in his 3rd week of the disease. He was discharged home on the 7th postoperative day. He was seen 6 months later and was in excellent health. Blood Hinton and Wassermann reactions were negative on two occasions at about that time. Serum agglutination tests of *Past. tularensis* were still positive in dilutions up to 1:320.

CASE 2. The patient (Rhode Island Hospital 375228), a 36-year-old loom fixer, entered the Rhode Island Hospital on November 16, 1943. For 4 days prior to the onset of his illness on October 28, he had spent part of the day hunting rabbits; he had killed ten, skinning and dressing them himself. At the time, he had a hangnail on the left thumb, and 1 day after the onset of the systemic illness the thumbnail became infected and the inflammation persisted despite treatment.

On the day of onset of his illness the patient was awakened at about 2 a.m. by chills and chilly sensations that continued the rest of the night. Alternating with the chills, he felt warm, perspired copiously and had a severe headache. The next day he noticed the infection near the left thumbnail, and within a short period of time observed sore lumps in the left axilla "as big as eggs." He called in his physician, who noted that he had a temperature of 104.5°F. For the 11 days until entry to the hospital, this fever continued rising, to 102 or 103°F. daily. Eight days prior to entry the patient developed a cough productive of moderate amounts of yellowish-white sputum without blood. This febrile illness, with malaise, headache, cough and the infected thumb and axillary nodes, continued up to entry.

On admission the patient had a temperature of 102°F. but did not appear acutely ill. Inspiratory rhonchi and wheezes were heard over the chest, with occasional rales at the left base. There was an ulcer at the angle of the nailbed of the left thumb that oozed serum, had black ragged edges, was tender and was surrounded by a tender area larger than the ulcer itself. There was a left epitrochlear node, and a plum-sized axillary node, both of which were nontender. The white-cell count was 14,700, with 43 per cent lymphocytes. A diagnosis of ulceroglandular tularemia was made, and the possibility of pneumonic involvement was raised. An x-ray film of the chest showed patchy density in both lobes compatible with bronchopneumonia. Agglutination tests done at the Rhode Island State Department of Health were positive against *Past. tularensis* in dilutions up to 1:80. Agglutination against brucella was negative.

On the 4th hospital day, with the patient continuing to run a temperature of 102 to 103°F. daily, sulfamerazine was given, beginning with a dose of 5 gm., followed by 1 gm. every 8 hours. After 3 days of treatment there was some improvement, but not until the 6th day did the temperature drop to normal. Coincident with this fall the pulmonary lesion cleared, and serum taken at that time was positive in titers up to 1:1280 and 1:2560. The thumb lesion was still unhealed and the axillary node was still enlarged and tender, with overlying redness in the skin. The patient was discharged 4 days later.

One week after discharge, the axillary node broke down and was incised and drained, and after 1 month it was slowly healing.† On December 21, 3 weeks after discharge and 2 months after onset, the agglutination tests against *B. tularensis* were positive in dilutions up to 1:2560.

During the hospital stay, cultures from the ulcer were injected into guinea pigs, which died and showed gross lesions characteristic of *Past. tularensis* infection. Bits of liver and spleen were cultured on cystine agar in an effort to isolate the organism, but the cultures were lost and the organisms were not finally identified.

†We are indebted to Dr. Wallace Lisbon, of Providence, Rhode Island, for information concerning the course of the patient after discharge.

DISCUSSION

Francis²⁰ has done much of the work on the etiology, transmission and animal vectors of tularemia, and his work should be consulted for these matters. A recent article by Foshay²¹ covers the clinical aspects, methods of early diagnosis and results of serum treatment. No attempt to review the literature will be made here.

Transmission from animals to man by insect bite is not uncommon.¹ The insect in Case 1 was most

known. One was the result of a cat bite, 1 of skinning a fox and 1 of handling an infected dog, and 3 were of unknown modes of transmission.

Of the 20 New England cases, 3 were fatal. One of the fatal cases was a pneumonic relapse from the ulceroglandular form¹⁵; the second showed a form of tularemia involving the lungs but apparently concomitant with an ulceroglandular lesion and at autopsy, lesions throughout the body¹⁶; in the third the disease was of the ulceroglandular variety

TABLE 1. Summary of 20 New England Cases of Tularemia.

YEAR	LOCALE	ANIMAL SOURCE OR INSECT VECTOR	TYPE OF LESION	BACTERIOLOGIC CONFIRMATION	OUTCOME	REFERENCE
1929	Boston (acquired in Georgia)	Tick	Ulceroglandular	Agglutination (1:1280)	Recovery	Withington ⁶
1929	Rhode Island	Rabbit	Ulceroglandular	Agglutination	Recovery	Randall ⁷
1929	Boston (rabbit from Illinois)	Rabbit	Ulceroglandular	Agglutination (1:640)	Recovery	Watts ⁸
1931	Claremont, New Hampshire	Rabbit	Unknown	None	Recovery	Badger ⁹ Eckstein ¹⁰
1933	Kokadjo Lake, Maine	Fox	Ulceroglandular	Culture, agglutination and autopsy	Death	Maine Department of Health and Welfare ¹¹
1935	Boston (acquired in Colorado)	Rabbit	Ulceroglandular	Agglutination (1:1280) and Foshay skin test	Recovery	Massachusetts Department of Public Health ¹²
1935	New Hampshire	?	Unknown	None	Recovery	New Hampshire State Board of Health ¹³
1936	New Hampshire	?	Unknown	None	Recovery	New Hampshire State Board of Health ¹³
1936	New Hampshire	?	Unknown	None	Recovery	New Hampshire State Board of Health ¹³
1937	Falmouth, Massachusetts	(?Rabbit) to Dog to Human	Typhoidal	Agglutination (1:1280)	Recovery	Badger ⁹
1938	Falmouth, Massachusetts	Tick	Ulceroglandular	None	Recovery	Massachusetts Department of Public Health ¹²
1938	Falmouth, Massachusetts	Tick	Ulceroglandular and pneumonic	Agglutination (1:1280)	Recovery	Moss and Evans ¹⁴
1940	Colchester, Connecticut	Rabbit	Ulceroglandular and pneumonic	Agglutination (1:640)	Death	Gibbons et al. ¹⁵
1941	Lawrence, Massachusetts	Rabbit	Ulceroglandular	Agglutination (1:640)	Recovery	Massachusetts Department of Public Health ¹²
1941	Rhode Island	Rabbit	Ulceroglandular	Culture and agglutination (1:2560)	Recovery	Eckstein ¹⁰
1941	Columbia, Connecticut	Cat	Ulceroglandular and pneumonic	Culture and agglutination	Death	Jungheer ¹⁶
1941	Stamford, Connecticut	Rabbit	Ulceroglandular	Agglutination (1:80)	Recovery	Connecticut Department of Health ¹⁷
1943	Falmouth, Massachusetts	Tick	Pneumonic	Agglutination	Recovery	Massachusetts Department of Public Health ¹²
1943	Waltham, Massachusetts	Tick(?)	Ulceroglandular	Agglutination (1:320)	Recovery	
1943	Providence	Rabbit	Ulceroglandular and pneumonic	Agglutination (1:2560)	Recovery	

likely the tick *Dermacentor variabilis*, which has previously been reported as the vector of Rocky Mountain spotted fever in New England.²² The tick *Dermacentor andersoni*, which is rarer in the eastern United States, may have been involved. The biting season of these ticks is from March to July. The other insect that carries the organism of tularemia is the horsefly, *Chrysops discalis*, which is active from June to September.

Many different animals have been found to be infected with tularemia, and the infection may be passed directly by handling or ingestion of the flesh, as well as by the parasites that are found on the infected hosts. Of the 20 New England cases, 9 involved direct handling of rabbits and 5 were traceable to tick bites, with the animal host un-

known. A tabular compilation of the pertinent data on the 20 cases is presented in Table 1.

Early diagnosis may sometimes be established by injecting material from the ulcer into a guinea pig, and then transferring bits of the necrotic foci in the liver and spleen to a cystine-containing medium.¹ The patient's blood culture may also be positive early in the disease, but again the organisms can usually be recovered only by animal passage. Francis²⁰ has pointed out that direct smear and culture are unavailing. Agglutination tests usually become positive from the third to the sixth week of the disease.

Foshay²¹ has described intradermal tests with suspensions of killed organisms in phenolized saline solution, which are read in forty-eight hours and

positive during the first week of the disease. It is also devised an intradermal test using anti-tularemia which is read in fifteen minutes and in one case has been reported positive as early as eight hours after the initial chill, but results have not been so successful as those with the vaccine. Foshay also developed an antiserum from goats and reported the results of treatment in 600 cases.

Case 1, the patient showed a false-positive skin test on two occasions. Six months after recovery, the serologic reaction was negative. Such a finding has not previously been reported, and its significance must await reports of other cases. Francis and Nagle²³ give the results of eighty-seven skin tests on 64 patients with tularemia; only "doubtful" reaction was obtained.

The response of the Massachusetts patient (Case 2) to primary excision of the ulcer was striking, and the results of this method are corroborated by other observers it may constitute a useful way of shortening the period of disability from the disease. He did not respond to sulfadiazine. An analysis of the response of the Rhode Island patient (Case 2) to a sulfonamide is difficult, since the dependence of temperature required six days after giving the drug.

SUMMARY

Eighteen cases of tularemia occurring in New England are reviewed. Of these, 8 have not previously been available in the literature. To these are added the detailed data on 2 New England cases, occurring in Massachusetts and 1 in Rhode Island during the summer and fall of 1943.

The mortality for this group of 20 cases was 15 percent.

Vermont remains as the only state in the Union where tularemia is endemic.

The false-positive Hinton test was a feature of the Massachusetts case. Clinical subsidence following excision of the ulcer was also an unusual feature of this case.

The Rhode Island case was one of ulceroglandular tularemia contracted from handling rabbits. In addition to local and lymph-node lesions, the patient

developed definite evidence of pneumonic involvement.

We are indebted to the following state officials for their willing aid in gathering together these data on tularemia throughout New England:

- Dr. Mary M. Atchison, acting state health officer, New Hampshire State Board of Health
- Dr. Charles F. Dalton, secretary and executive officer, Vermont Department of Public Health;
- Dr. Roy E. Feemster, director, Division of Communicable Diseases, Massachusetts Department of Public Health;
- Dr. Roscoe L. Mitchell, director, Maine Department of Health and Welfare;
- Dr. Stanley H. Osborn, commissioner, Connecticut State Department of Health; and
- Dr. William P. Shields, epidemiologist, Division of Communicable Diseases, Rhode Island Department of Health.

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VITAMIN B DEFICIENCY IN PRIVATE PRACTICE*

DUDLEY MERRILL, M.D.†

CAMBRIDGE, MASSACHUSETTS

PURE, uncomplicated diseases caused by deficiency of vitamin B—pellagra, beriberi, ariboflavinosis, polyneuritis and the Wernicke syndrome—are a great rarity in New England. This is probably true in most geographical areas where famine is unknown and the dietary habits of the majority of the people are not rendered grossly inadequate by poverty or by the lack of coarsely ground cereals, green vegetables, dairy products and meat. Occurring as complications of many different types of disease, however, these diseases are being recognized with increasing frequency and are actually of far greater importance clinically, outside the endemic areas of pellagra and beriberi, than are their uncomplicated forms.

Cowgill¹ demonstrated that the tendency to develop symptoms of vitamin B deficiency varies with the metabolic rate of the body and inversely with the vitamin B intake, and that the body weight and metabolism are consequently the most important factors determining the vitamin requirement. From these fundamental laws he was able to predict or explain the clinical occurrence of vitamin B deficiencies in association with many widely different types of disease. Shattuck,² Wechsler,³ and Minot, Strauss and Cobb⁴ had already reported beriberi complicating polyneuritis in patients suffering from profound nutritional disturbance, either alone or as a complication of many types of chronic illness. Strauss and McDonald⁵ had also pointed out that the polyneuritis of pregnancy, previously attributed to a hypothetical toxin, is in all probability merely another example of polyneuritis due to a nutritional deficiency. In a later paper, Strauss⁶ elaborated on the importance of disturbance of the gastrointestinal tract as a conditioning factor in the production of deficiency states. Weiss and Wilkins,^{7,8} reported beriberi heart disease as not infrequent in patients suffering from nutritional deficiency.

From the work of all the above authors it has become apparent that clinical manifestations of vitamin B deficiency should be searched for in any situation in which there is an increased metabolism, with or without an obvious deficiency of vitamin B in the diet or a disturbance of the function of the gastrointestinal tract. This may arise because of increased muscular activity, increased caloric intake, fever, hyperthyroidism, long-continued vomiting, diarrhea or dietary restriction.

It is unfortunate that in this group of cases there is great danger of overlooking the earliest symptoms

and signs of impending deficiency disease because of the frequently far greater importance of the precipitating factor—pneumonia, malaria, cirrhosis of the liver, pregnancy and so forth.

Many authors have stated that the earliest manifestations of vitamin B deficiency are easily reversible if proper therapy is instituted, whereas later process may progress to a stage of slow reversibility or nonreversibility in spite of substitution therapy.

I⁹ have already reported 3 cases of severe dysphagia associated with profound nutritional deficiency, 1 of them mistakenly diagnosed as carcinoma of the esophagus, all of which responded to substitution therapy. In retrospect the response to therapy—perhaps be explained by the short duration of symptoms.

Goldsmith¹⁰ searched for evidences of riboflavin and niacin deficiency in a series of 200 consecutive patients admitted to the medical services in the Charity Hospital in New Orleans; these consisted of 50 white women and 50 Negroes, and 50 white men and 50 Negroes. She found 79 cases of definite and 54 of probable deficiency disease in this unselected series. It may be considered by some of her criteria for diagnosing these deficiency syndromes were slightly overgenerous, but there can be no doubt that these diseases were of far greater prevalence in this particular group of charity patients in a Southern city than even most nutrition experts would have expected.

Because of the frequency with which cases of vitamin B deficiency of moderate or severe nature have appeared in private practice in the metropolitan area of Boston, it has seemed worth while to report some of them. These diseases are not limited to any special group,—to the natives of Labrador or the Orient, sharecroppers, chronic alcoholic addicts or the inmates of a city hospital. Furthermore, they are common complications of many serious illnesses, and their recognition is not purely of academic interest. The therapeutic implications are obvious.

CASE REPORTS

CASE 1. C. J. M., a 63-year-old widow, was first examined because of asthma, cough and vomiting. Three days previously she had had severe chilly sensations, cough and a pain in the chest. Asthma, which she had had off and on for 25 years, returned. For 3 days she had vomited practically everything she had eaten. A year and a half before this episode she had been diagnosed as having malnutrition and dactylitis, but in spite of much dietary advice she had failed to put on any weight.

Physical examination revealed a temperature of 103°F., a pulse of 120 and a blood pressure of 130/80—18 months previously it had been 200/110. The lungs were full of asthmatic rales, but there was a patch of pure bronchial breathing over a small area of the right upper lobe anteriorly.

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

†Instructor in medicine, Harvard Medical School; junior visiting physician, Boston City Hospital; associate physician, Cambridge Hospital.

The patient was hospitalized at once. The sputum contained Type 2 pneumococci, and x-ray examination of the chest showed consolidation in the right midlung. The blood protein nitrogen level was 67 mg. per 100 cc. but fell to 7 mg. 2 days later. Sulfathiazole was given for 3 days, the temperature fell to normal in 24 hours. Five days after admission she developed urinary retention, with a nonprotein nitrogen of 75 mg., and exhibited considerable mental confusion. For the next 3 days the patient was repeatedly catheterized and fluids were given in large quantities, but the nonprotein nitrogen level rose to 100 mg. and she developed sacral and pulmonary edema, with profuse sputum and a beefy-red tongue. She was given 100 mg. of nicotinic acid every 3 hours and 2 cc. of mercupurin intravenously, and fluids were limited to 2000 cc. every 24 hours. An indwelling catheter was placed in the bladder. Twelve days after admission the nonprotein nitrogen level had fallen to 25 mg. and the temperature to below 100°F. The patient was well oriented, the edema had disappeared, and the tongue was practically normal. The bladder control did not return to normal for another 4 weeks. The patient was discharged 6 weeks after admission.

This sixty-three-year-old undernourished, asthmatic woman developed pellagra ten days after the onset of pneumonia and five days after the temperature had returned to normal. She finally recovered from both the pellagra and the pneumonia.

Of considerable interest is the fact that she survived a second attack of pneumococcal pneumonia exactly two years after the one reported here. She was treated with sulfadiazine and large amounts of vitamin B complex from the onset, and experienced no complications.

CASE 2. M. P., a 68-year-old edentulous widow, was seen because of an extremely sore mouth. One month previously she had had pneumonia with moderately severe jaundice. She had received no serum, and sulfonamide drugs had been withheld because of the jaundice. She ran a course characteristic of pneumonia and improved. The temperature became normal 16 days after the onset of the pneumonia. Twenty days after onset, she first complained of a sore mouth. A severe stomatitis was noted and sulfanilamide was prescribed. Three days later the mouth was full of so-called "Vincent's lesions," which were painted with 10 per cent chromic acid.

When I first saw the patient 12 days after the onset of stomatitis, the tongue was smooth, moist and fiery red along the edges. Toward the back there was a sharp line where the exfoliation had apparently stopped. There were two ulcers 3.5 cm. in diameter inside the right cheek and extending over the toothless lower gum. They were filled with blackish slough, the result of cauterization with chromic acid. The entire mouth and lips were extremely sore, and there were several small ulcers in both tonsillar regions and on the floor of the mouth. There was no dermatitis of the hands or legs, and no neuritis. A diagnosis of stomatitis due to acute vitamin B deficiency secondary to pneumonia was made, and the patient was started on 100 mg. of nicotinic acid and 4 brewer's yeast tablets three times a day. Local treatment was limited to a saline mouthwash.

Eleven days after the beginning of vitamin therapy the stomatitis had improved strikingly, although the left side of the throat was still sore. The ulcers inside the right cheek were one third their former size, and those in the tonsillar regions and on the floor of the mouth were clean and beginning to heal. The patient had some difficulty in mental concentration, some numbness of the right leg and soft and pitting edema of both legs up to the knees. At that time it was discovered that she had had peculiar dietary ideas for some years, having avoided all meats, drunk little milk and eaten only a few eggs for months, if not years, before the onset of pneumonia. Additional diagnoses of peripheral neuritis and probable protein deficiency were made, and the patient was urged to alter radically her eating habits.

When last seen 6 days later, the patient was feeling much better. The throat and mouth were no longer sore and she

was eating well. She was having less difficulty with mental concentration, all the ulcers in the mouth were healed except one inside the right cheek, which was still 1 cm. in diameter, and the edema and the numbness of the right leg had disappeared.

This elderly edentulous woman with peculiar eating habits developed clinical pellagra, beriberi and probable protein deficiency following a moderately severe pneumonia. It seems likely that if the course of the pneumonia had been cut short by either drug or serum therapy, — jaundice complicating pneumonia is now known not to be a contraindication for either, — she might never have manifested outspoken signs of vitamin B or protein deficiency, in spite of her inadequate dietary and poor dental equipment.

CASE 3. P. R., a 47-year-old, married woman of a slender, apprehensive type, was seen because of metrorrhagia. A uterine curettage 2 months later showed hypertrophic endometrium but no signs of malignancy. A hysterectomy was performed. Five days after operation the patient began to be nauseated and vomited several times. This continued for several days and the patient became extremely depressed. She had eaten almost nothing since the operation. The temperature had remained flat the first week after operation, never going above 99.6°F., but the pulse had slowly risen to 110. The patient was dehydrated, but the tongue aside from being dry appeared perfectly normal, being neither sore nor red. The possibility of vitamin deficiency and gastric dilatation was raised. Thiamin chloride and intravenous glucose and saline solutions were started and a tube was inserted in the stomach. One thousand cubic centimeters of black, foul-smelling liquid was removed and the patient felt better. The next day she had several loose stools and the tongue was still dry, so that more intravenous glucose and saline solutions were given. Another gastric lavage produced a large amount of green, foul-smelling fluid.

Nine days postoperatively, diarrhea was well established and the administration of 100 mg. of nicotinic acid every 4 hours was begun. On the 4th day, the patient looked better and the nausea, vomiting and diarrhea had stopped, but the mucous membranes of the entire inside of the mouth and tongue began to peel off. From time to time she was confused, irritable and difficult to handle, being extremely suspicious of visitors, nurses and doctors.

By the 12th day, the mental state seemed to be clearing, although the patient was still having three or four loose stools a day and occasionally vomited undigested food. By the 14th day she seemed mentally normal, the diarrhea had diminished to one or two loose stools a day, and vomiting had ceased. The temperature was normal and the pulse 90, and the oral mucous membranes were no longer fiery red or sore.

The patient again became psychotic on the 17th day, refusing all medication. On the 20th day, although progressing satisfactorily, she was still restless at night and developed an itching, erythematous eruption of both shins and the skin at the base of the neck. The lips were still dry and peeling and there was a small crack at the left commissure.

By the 26th day, the patient was practically well. The dermatitis, stomatitis, diarrhea, psychosis and tachycardia had all cleared. On close questioning it was found that during the 6 weeks between the time she was first informed that she would probably have to have an operation and its actual performance she had been so worried about the operation and its attendant risks and discomforts that she had eaten poorly.

This thin, anxious, forty-seven-year-old woman developed classic pellagra with diarrhea, dermatitis, stomatitis, psychotic manifestations and tachycardia during an afebrile postoperative course as the result of poor eating habits for six weeks prior to operation and practical starvation for the first

week after it, the deficiency of vitamin B being further accentuated by intravenous infusions of glucose solutions (cf. Cowgill's caloric vitamin B ratio¹). One may speculate whether the tachycardia was due to thiamin deficiency although it is only of academic interest, since the patient obviously suffered from a niacin deficiency and there was almost certainly an associated thiamin deficiency.

Incidentally, it is also possible that vitamin B deficiency may be a contributory factor in some cases of postoperative gastric dilatation, intestinal distention and ileus and impaired bladder function.

CASE 4. H. C., a 69-year-old woman physician, was a chronic alcoholic and morphine addict. She had had so-called "colitis" for 10 years and had been diagnosed as having pellagra 5 months before I first saw her. She had been giving herself parenteral injections of a preparation of vitamin B complex since the diagnosis of pellagra had been made, but had continued her morphine and alcohol habits. She was seen in consultation because of cardiac failure. She was found to be obese, to have pinpoint pupils, — the result of morphine, — a severe glossitis, scaling and discoloration of the skin of the lower legs and roughness of the skin on the backs of the hands. The skin of both thighs showed innumerable scars of hypodermic injections. The heart was fibrillating (rate, 120), the blood pressure was 125/100, and there were signs of congestive failure. There were no murmurs, but the examination of the heart was not satisfactory owing to poor co-operation. The liver was felt two fingerbreadths below the costal margin. The reflexes were equal and active, and there was no tenderness on firm pressure on the calves.

Diagnoses of obesity, cardiac failure, morphinism, alcoholism and mild pellagra were made. The patient was rapidly digitalized and the previous dose of parenteral vitamin B complex was trebled. Three days later, when the heart rate was well controlled, she became completely disoriented. The daily morphine allowance was reduced, but she became psychotic and developed an intractable diarrhea. Although diarrhea is accepted as a common manifestation of withdrawal of morphine, there seemed to be an equal possibility that vitamin B deficiency was a contributory factor, so that 100 mg. of nicotinic acid was given by mouth every 2 hours. Two days later the patient was mentally clear, but the loose stools continued.

This obese sixty-nine-year-old woman, who was addicted to alcohol and morphine, had both severe cardiac failure and relatively mild pellagra. With adequate digitalization and gradual withdrawal of morphine she became psychotic and had severe diarrhea. The suggestion is made that one or both of these symptoms were manifestations of the pellagra, perhaps accentuated by the rapid restoration of cardiac compensation. One wonders whether some of the so-called "digitalis toxic psychoses" that appear in chronically decompensated cardiac patients, usually coincident with or immediately following a rapid diuresis and clearing in a few days' time with improvement of the cardiovascular status and ability to eat, may not be largely due to vitamin B deficiency.

Cowgill¹¹ showed that in dogs a diuresis produced by feeding large amounts of water by stomach tube hastens the time of onset of the anorexia characteristic of a deficiency of the vitamin B complex. His explanation is that significant amounts of vitamin B are carried off in the increased urinary output.

If the concentration of vitamin B in edema fluid is significantly less than that in the circulating blood, a diuresis produced by digitalis or mercurial diuretics might well be expected to hasten the development of clinically apparent vitamin B deficiency.

CASE 5. S. C., a 57-year-old man, was seen at home complaining of pains in the legs and back and diarrhea of 2 months' duration. One year previously he had had intestinal obstruction, and at operation a carcinoma of the colon was found. The entire right colon was resected. He gained strength and felt extremely well for the next 10 months, but intestinal obstruction recurred and a second operation revealed extensive intra-abdominal and intrahepatic metastases. A short-circuiting operation was performed, but the patient had had diarrhea steadily ever since. He had also had considerable pain in the right lower quadrant of the abdomen and had taken a great deal of codeine in an attempt to control it. He had recently shifted to morphine by mouth but was still having three to five stools a day and considerable aching in the legs and back. X-ray films taken the preceding week had shown no changes in the spine, pelvis or femur. He had lost about 25 pounds in the preceding 2 months, but still weighed about 200 pounds.

Physical examination showed a well-developed and fairly well-nourished man who gave evidence of recent weight loss. The tongue and mouth were normal. There were multiple hard masses throughout the abdomen, and the liver was felt at the level of the umbilicus.

A week later, in addition to having diarrhea, the patient began to vomit two or three times a day. Two weeks after the first examination the tongue was noted to be fiery red and dry. The vomiting and diarrhea continued. Three days later the mouth became sore, and a week later it showed many shallow ulcerations. No attempt was made to give parenteral nicotinic acid, thiamin or vitamin B complex. It was impossible to determine how much of the pain was due to neuritis secondary to the vitamin B deficiency or how much to the known extensive carcinoma. Cure was impossible, so that only palliation was attempted in the last weeks of life.

This fifty-seven-year-old man, who had extensive metastatic carcinoma of the liver and peritoneal cavity, a short-circuiting bowel operation and diarrhea of two months' duration, developed pellagra in the last two weeks of life. Profound malnutrition from chronic diarrhea, vomiting and extensive metastases in the liver were contributory factors.

CASE 6. A. F. M., a 72-year-old woman, was seen in 1936 because of an extremely sore tongue of at least 5 years' duration. Three years previously she had been minutely studied in a teaching hospital because of the same complaint. Most of the time she was overweight, spoon-shaped fingernails and a smoky, shiny, red painful tongue were noted. Blood studies ruled out both pernicious anemia and hypochromic anemia, and no clue to the painful glossitis was discovered. All the time she had been extracted some years previously, and double dentures had been worn ever since.

In 1936 the tongue still looked the same as it had in 1933, with the exception that there were some small superficial ulcerations at its tip. With the findings of Blankenhorn¹² in mind, a diagnosis of glossitis from vitamin B deficiency was made. A careful dietary history revealed marked meat deficiency since the teeth had been extracted and a partiality for white bread.

During the next 2 years, tablets of brewer's yeast, nicotinic acid and riboflavin were administered in large amounts with no apparent effect except a mild psychologic improvement. Finally, because of obvious failure to influence the patient's affliction therapeutic attempts were abandoned for 4 years. In 1942, the patient began to lose weight at an alarming rate. There were few symptoms except the earlier on sore tongue, increasing difficulty with vision owing to cataracts, shortness of breath, and general weakness attrib-

teriosclerotic heart disease. Extensive x-ray studies had no evidence of organic disease other than arteriosclerosis. The patient's own physician finally decided to try intramuscular injections of liver. The result was miraculously. From the date of the first injection she began to improve. The first symptom to disappear was the sore tongue, which had been present almost continuously for 11 years. She next developed a ravenous appetite. In the next 6 months she gained 20 pounds, and although she had been expected to survive the winter, she became strong and well.

This elderly woman with double dentures had had painful glossitis for eleven years that failed to respond to yeast, nicotinic acid and riboflavin by mouth but improved miraculously after injections of liver extract. Apparently the glossitis was of the type seen in sprue and pernicious anemia, which, as shown by Castle and his co-workers,¹³ responds to liver extract orally or parenterally but not to orally administered components of the vitamin B group. Of considerable theoretical interest is the fact that even after eleven years the glossitis was still a reversible process and was completely relieved by the intramuscular injection of liver extract.

It seems not unlikely that a certain number of the symptoms usually associated with advanced age — mental confusion, loss of memory, disorientation at night, mildly paranoid ideas, asthenia, loss of appetite, weight loss and neuritis or rheumatic pains — are partially caused by vitamin B deficiency and not, as is usually assumed, solely by cerebral arteriosclerosis.

CASE 7. H. D., a 38-year-old farmer and shipyard worker, with an unusually strong frame and a tremendous capacity for hard manual labor, had had pains in the forearms and hands for about 6 months, and cramps in the forearms sometimes kept him awake at night. Every morning it took him some time to limber up his fingers. Milking became extremely painful and using a hammer for more than an hour, as in shingling or caulking, became an impossibility. The hands and arms had never been frozen and the patient had not been exposed to lead paint or lead fumes for any period of time; he took alcohol only on rare occasions.

Physical examination showed a robust, red-checked, extremely healthy-looking man weighing about 200 pounds. He carried 10 to 20 pounds of extra fat. The tongue was entirely normal, and the rest of the examination was negative. There was no demonstrable weakness of the muscles of the hands or forearms, and all the reflexes were normal.

Questioning as to diet revealed a special liking for potatoes, of which the patient ate six or eight a day, and white bread and a distaste for meat. His daily schedule involved getting up at 6 a.m., doing the milking and farm chores, working at a shipyard from 8 a.m. to 4 p.m., resuming his farm work, delivering milk and getting to bed between 11 p.m. and midnight.

On the remote chance that the pains were due to neuritis arising from a relative vitamin B deficiency caused by the enormous total metabolism, high-starch diet and low intake of vitamin B, 9 capsules of vitamin B complex were given daily by mouth and the patient was advised to take less potatoes and white bread. In 6 months the paresthesias had disappeared and the patient regained full use of his hands and arms.

This extremely vigorous, active, overweight farmer and shipyard worker, who averaged fourteen to eighteen hours of physical labor daily, developed a severe neuritis of both forearms and hands interfering seriously with his work. His diet was high in

calories and starch and relatively low in foods containing vitamin B. His neuritis cleared up when his diet was corrected and supplements of vitamin B were added.

Obesity was possibly a minor contributory factor to the dietary deficiency in this case. It may contribute to vitamin B deficiency because it is always associated with an increase in total metabolism (Newburgh¹⁴), and because the more obese a person is the more likely his caloric vitamin B ratio (Cowgill¹⁵) to be deficient. Adiposis dolorosa (Dercum's disease¹⁶⁻¹⁸), with its asthenia, neuritis and psychosis, sounds suspiciously like an extreme example of obesity predisposing to vitamin B deficiency.

CASE 8. E. G., a 22-year-old stenographer, was seen with typical scarlet fever on the 3rd day of her illness. It had begun as an extremely sore throat. The patient had had great difficulty swallowing even fluids. The temperature was 105°F. and the pulse 130. The throat showed extensive exudate on both tonsils, and the right tonsil was pushed forward. There was a typical scarlatiniform eruption. The heart had no murmurs, and there was no history of rheumatic fever, chorea or a previous peritonsillar abscess.

The patient was hospitalized the next morning and was given antitoxin and sulfamerazine because she was extremely toxic. One day after admission the blood sulfamerazine level was zero, probably owing to an accidental confusion of blood samples, so that the drug was continued in full doses. The next day the level was 29 mg. per 100 cc. and the patient had oliguria. The drug was stopped and she was given glucose and saline infusions. Four days later the temperature fell to 100°F. Large quantities of urine were being excreted, but the patient had paranoid ideas, a gallop rhythm and what some observers called a pericardial friction rub but which I interpreted as a contact sound. At that time she looked a great deal better than she had when first seen 6 days before. The throat was much less sore, and she was able to swallow without much discomfort. The right tonsil was still pushed forward. There was fissuring at the outer corners of the eyes and lips. The tongue was smooth and red, with occasional enlarged papillas protruding above the surface. The heart was rapid and regular at a rate of 120/140, and the temperature was still 100°F. There was a well-marked gallop rhythm, and the above-mentioned scratchy sound was synchronous with both the 1st and 2nd sounds at the lower end of the sternum.

On the basis of paranoid ideas, cheilosis and embryocardia with gallop rhythm, a diagnosis of acute vitamin B deficiency was made. The contributory factors were sepsis, fever, inability to eat solid food for 8 days and intravenous infusions of glucose solution. A cardiac consultant made a diagnosis of acute rheumatic myocarditis and pericarditis, and the visiting physician a diagnosis of scarlet-fever heart.

The patient improved rapidly from this time on, having begun to eat well. The next day, she became and remained mentally clear, the heart began to slow down, and the friction rub disappeared almost at once.

Fifteen days after the onset of scarlet fever a peritonsillar abscess on the right ruptured spontaneously. At that time there were also migratory transient joint pains, with slight redness and limitation of motion for a few days. The electrocardiogram never showed a PR interval greater than 0.18 second, and all tracings showed a tendency to slight right-axis deviation. A soft apical systolic murmur developed, and the sedimentation rate was two or three times normal.

From the 17th day of the illness there were no further joint pains, fever or any other symptoms. The convalescence was uninterrupted. The sedimentation rate finally became normal 2 months after the first symptoms. When the patient was last seen, 10 weeks after the onset of the scarlet fever, the examination of the heart was entirely normal except for a faint apical systolic murmur, which was heard only when she was lying down and disappeared on exercise.

This healthy young woman with no previous history of rheumatic fever or any other type of heart disease developed paranoid ideas, cheilosis and tachycardia with gallop rhythm eight days after the onset of severe scarlet fever. The acute vitamin B deficiency was precipitated by fever, sepsis, inability to eat and intravenous infusions of glucose solution. It is impossible to establish an exact diagnosis of the cardiac lesion. Unfortunately, there are no pathognomonic signs or laboratory tests for differentiating or diagnosing some cases of rheumatic myocarditis, beriberi heart and scarlet-fever heart.

Wesselhoeft,¹⁹ from his extensive experience with scarlet fever, describes scarlet-fever heart as a transient affair lasting for a few days to three weeks. It usually consists in the development of murmurs, without irregularity in rhythm. The first sign is generally a split first sound. Abnormalities are likely to be noticed when the patient is first allowed out of bed. The murmur is extremely variable in time and character. It may occur in systole or diastole, but more frequently in the former. Some writers have emphasized that its occasional harshness is somewhat suggestive of a slight friction rub at the base. The heart rate is not necessarily increased with the advent of these abnormal sounds, but quite independently of them there may occur a persistent tachycardia or even a relative bradycardia. There is rarely any cardiac enlargement, and there is no precordial pain or discomfort. All these clinical signs usually disappear by the end of a week, and in marked cases in three or four weeks. Electrocardiographic changes are variable, inconstant and nonspecific.

A similarity may be seen in this description between scarlet-fever heart and the milder forms of beriberi heart disease (Weiss and Wilkins⁹). There are no clinical or laboratory tests that distinguish between them with certainty. The suggestion is made that they may be identical conditions. The excellent prognosis of practically all cases of scarlet-fever heart may be explained by the fact that once the acute sore throat of scarlet fever subsides the patient begins to eat. Also, the normal nutritional status of most persons preceding an attack of scarlet fever renders them less likely to develop the more advanced stages of beriberi heart disease.

CONCLUSIONS

The above 8 cases of clinical vitamin B deficiency were seen in seven years of private practice. They have been reported in the hope of emphasizing the frequency with which this group of diseases occurs as a complication of many serious illnesses seen every day in practice. Therapy is self-evident if

the diagnosis is made. An acute awareness of the existence of such conditions is necessary if the cases are to be correctly diagnosed and treated their earlier stages.

The precipitating or contributory factors in the small series were fever, a bizarre diet, chronic diarrhea, poor teeth or poorly fitting dentures, operative apprehension, infusions of glucose solution, hard manual labor, obesity, drug addict diets rich in starch and sore throat or sore mouth. In any given case there was usually more than one factor.

It may be repeated that symptoms of vitamin B deficiency may develop whenever an elevated metabolism occurs simultaneously with a deficiency of vitamin B-containing substances in the diet or any interference with absorption in the gastrointestinal tract. These should be looked for in cases of fever, increased caloric intake, increased muscular activity, hyperthyroidism, chronic diarrhea or vomiting and the like, with or without obvious limitation of intake or absorption of vitamin B-containing foods.

51 Brattle Street

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THE PURPOSE AND ACCOMPLISHMENTS OF THE LAWRENCE CLINIC

H. FRANK MCCARTHY, M.D.,* AND FREDRICK C. ATKINSON, M.D.†

LAWRENCE, MASSACHUSETTS

1936, one of us (H.F.M.) became convinced, through observations made during the course of practice, that there should be in Lawrence an institution devoted primarily to the care of the socially indigent. It was noted that because of the lack of adequate outpatient facilities, poor patients were prone to employ a physician or surgeon until accumulated bills became prohibitive, and then, because of inability to pay the incurred debt, "passed" from physician to physician. Because of numerous experiences of this sort, it was obvious that there was an urgent need for this charitable institution. Accordingly, the interest of the late W. Dacre Walker, a physician of influence and high repute in this community, was enlisted, and after considerable study and thought he gave the subject his wholehearted support. Dr. Walker became the first president of the Board of Trustees and the first chief of staff.

On November 13, 1936, the charter was granted and a group of outstanding lay persons consented to act as trustees. A meeting was held by nine representative physicians and dentists of the community and plans to open a free outpatient clinic were formulated. Aided by funds and equipment donated by these physicians and dentists, on January 6, 1937, the clinic made its inauspicious start, poorly housed in a somewhat dilapidated local building. A certain amount of criticism, which is usually attendant on an innovation, was at first directed toward the clinic, owing to the mistaken impression that its primary purpose was the financial gain of its sponsors. Criticism abated and suspicions were allayed once the public became convinced of the worthiness and sincerity of the project.

It was early recognized that the services of the clinic would be sought by many who could afford private care. Accordingly, rigid rules for admission were devised. It was decided that candidates for the clinic should be admitted only on the presentation of a reference from a physician, dentist, minister or recognized charitable agency, stating that the bearer could not afford to pay for private care. In a few cases it was found that the referrer had recommended patients who were not financially deserving of clinic care. They were warned, and if the offense was repeated their privilege to refer patients was revoked. Again, on a few occasions it was found that physicians referred patients for special work, such as laboratory or x-ray examination, who were not eligible, but when it was explained to them

that patients must also be of clinical status to receive this care, the difficulty was eliminated.

SOCIAL RELATIONS

The case load in the early days of the clinic was extremely heavy because of conditions in the mills following the Depression. Recently, with the advent of war production, the load has dropped considerably and, for the first time in many years, people who were formerly on the relief rolls and had received free care at the clinic have become contributors to its support. This point is important, since in a community of the type of Lawrence the borderline between prosperity and poverty is frequently the holding of a job. In the files of the clinic are hundreds of letters of gratitude written by former patients who wish it to be recognized that they have now assumed the role of givers rather than receivers.

The clinic is at present maintained by public donations, which are solicited by mail. About \$10,000 is received yearly from approximately 3000 donors. There are a few large annual donations made from several organizations, but it is apparent from these figures that the bulk of the money received is in small amounts and is sent from a cross section of the working people of the community. A survey of the list of donors is convincing proof that the clinic is being largely supported by potential patients, and a great many of their letters indicate that they are cognizant of this fact.

STAFF

The original charter members interested other members of the medical profession in the project. These physicians and dentists staffed the various departments and have given generously of their time year after year, with no remuneration other than the gratitude of the patients. Many of the original staff were young men, not too busy in their private practice and not at the time affiliated with any other local institution, so that they could afford to spend considerable time when the medical case studies were to their professional advantage. For the cases that require special study, ten outstanding Boston specialists act as consultants to the various departments, and the clinic has been accorded the privilege of referring to them such patients as require their attention. These men, also, have worked without financial remuneration.

As in other instances, the war has brought special problems to this institution. As stated above, the clinic was originally staffed almost wholly by youthful physicians and dentists. Now that the various

*Chief-of-staff, Lawrence Clinic.

†Head of Medical Department, Lawrence Clinic.

branches of the service have recruited most of them, out of the original staff of fifty-two only nine are now active at the clinic. These men, however, can adequately handle the work because of the lighter case load resulting from improved economic conditions.

ADMINISTRATION

The number of paid workers at the clinic is eight, consisting of a superintendent, a secretary-bookkeeper, a clerk, a laboratory technician, a medical assistant, a registered nurse, a dental hygienist and a janitor. These paid workers, however, are augmented by numerous volunteer workers in all departments from office work to medical assistance. Most of the administrative staff are underpaid in comparison to their efforts, but have stayed on in spite of opportunities for higher pay, feeling recompensed by the satisfaction that comes to those who render a community service. Through the kindness of a prominent local accountant, a bookkeeping system was installed, and this is audited yearly without charge.

FACILITIES

In April, 1940, after three years of operation in humble surroundings, the clinic moved to its present location. Under the supervision of the Board of Trustees, the building in which it is now housed was purchased, and although heavily mortgaged at the time of purchase, it was possible to renovate it completely and to equip each department with the most modern equipment. The rooms, which are clean and wholesome, are unpretentious and strictly utilitarian. Most of the available money was expended on good medical equipment rather than in beautifying the surroundings. This, in the opinion of the staff, was much more advantageous to the patients' welfare. All departments are well equipped, and they include a dental clinic with two chairs. Some of the departments are supported by various organizations, as in the case of the Eye, Ear, Nose and Throat Department, which is sponsored by the local Lions Club.

Medicine is dispensed free or at cost. In 75 per cent of the cases it is given without charge. Appliances such as arch supports, eyeglasses and back braces are obtained for patients at cost, but if the latter are unable to pay even this amount, an endeavor is made to procure the appliances through some welfare organization. As a last resort, the clinic will purchase such appliances for a worthy patient.

When a patient needs hospitalization for surgery, efforts are made to secure a free bed in a private hospital, and the clinic's staff surgeons do the operating without charge. In certain cases patients are referred to the municipal hospital.

Among other facilities available to patients: completely equipped x-ray department. Here the patient if financially able pays the exact amount of the material used. If he is unable to pay, work is done free. The clinic has a well-equipped laboratory with a competent technician in charge.

In June, 1938, a state venereal-disease clinic was assigned to the Lawrence Clinic. Needless to say, this is always one of the busiest departments. The State reimburses the clinic on a per capita basis for each patient treated, and although no results from this arrangement, it makes this particular department self-supporting.

On first admission, a patient is requested to pay an admittance fee of 50 cents, and 25 cents for each successive visit. The admission fee was decided upon as a morale factor and for its psychological effect on the patient rather than for the financial return expected from it. About 65 per cent of the patients are unable to pay even this small fee and are admitted free. Their ability to pay or to receive free care is determined on the first admission by the admitting clerk. The economic status of each patient is watched as carefully as possible, and improvement in such status, the patient is urged to return to his family physician for medical care when he again becomes eligible for clinic care.

LADIES' AUXILIARY

Shortly after the opening of the clinic, civic-minded women volunteered their services to the institution in various ways. They often drove elderly patients to and from their homes, made medical supplies, sewed curtains and in many other ways assisted in the undertaking. This group was the nucleus of a larger group of women who formed the Ladies' Auxiliary. This auxiliary has been invaluable to the clinic. Its members have sponsored benefit parties and have raised considerable sums of money. They have been to a great extent a factor in promulgating goodwill throughout the community and in helping to dissipate any latent suspicions that might still be entertained regarding the purpose of the institution.

* * *

The clinic is about to enter on its seventh year of service to the medically indigent of Lawrence and the surrounding communities. During the past years approximately 100,000 treatments have been received by these people. If it is borne in mind that all the patients have been bona-fide charity patients it will be realized that the institution has justified its existence and established its position as a social necessity. If in this period only a few human beings had been rehabilitated, — and there have been hundreds, — the sponsors of the clinic would still find that the end had been worth the means.

MEDICAL PROGRESS

PIGMENTATION OF THE SKIN (Concluded)*

HAROLD JEGHERS, M.D.†

BOSTON

MELANOSIS ASSOCIATED WITH AN INCREASED NUMBER OF MELANOBLASTS

BECKER and Obermayer¹⁰² classify a number of pigmentary disturbances as melanosis associated with an increased number of melanoblasts (Table 2). Some of these are of general medical interest. The increased melanoblasts of the blue nevus (see colored plate³⁰⁵) and of Mongolian spots (see colored plate²⁸) are deep in the corium, so that the resulting melanin pigmentation appears blue. Blue nevi bear the same relation to Mongolian spots as the ordinary brown moles do to brown-pigmented skin.³⁰⁶ Mongolian spots are frequently noted over sacral and other areas in the darker races and occasionally in the white-skinned races, and persist for a variable number of years after birth.³⁷

Ephelides (freckles)^{11, 22, 102, 103} are due to increased aggregates of melanoblasts producing accentuated, sharply demarcated yellowish-brown areas, often zizzag in outline. They are more obvious in spring and summer, can be seen with Wood's light when invisible to the naked eye (see illustration³⁰⁷), appear early in life but not in infancy, never occur on the palms and soles and are prominent on the exposed parts of the body, and the predisposition to them is an inherited dominant characteristic. They may be confused with lentigo and melanosis produced by disease.

Melanotic neoplasms of the skin are frequently encountered. The difficulty of treating them and the frequency of metastasis from them are well known. Of significance here is the observation that aside from true metastases, malignant melanoma may cause a diffuse and marked melanin pigmentation of the skin.³⁰⁸⁻³¹⁰ In a reported case (see illustration³⁰⁸) a white man became so dark in color that he was thought to be a Negro.

Sharply outlined brown blotches, *café au lait* spots and large areas of brown skin pigmentation (see illustrations^{311, 312}) are among the commonest features of neurofibromatosis (Recklinghausen's disease), and in some reported series were noted in every patient.^{311, 313} The pigmented spots are usually not congenital and may develop in childhood or later in life. The pigmentation in this disorder is considered to be due to a localized anatomic anomaly

in the cutaneous nerve itself that produces the increase of melanin in the epidermis.³¹³ In its classic form neurofibromatosis is readily recognized. It is, however, not well appreciated that in the formes frustes^{312, 313} pigmented spots on the skin may be the only visible manifestation of the disorder. It is now well known that neurofibromatosis may involve many internal organs, including the bone, the central nervous system, and the endocrine organs, and it is therefore of general medical interest.^{312, 314} The possibility of neurofibromatosis should not be overlooked in persons with patches of brown skin pigmentation of this type.

Much interest has been aroused in recent years in a curious syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and a gonadal dysfunction, especially precocious puberty in the female.^{315, 316} It has been referred to in the recent literature as osteitis fibrosa cystica (Albright) and Albright's syndrome. The disorder is not due to parathyroid disease. The patchy skin pigmentation seen in this disorder is almost constantly present, is brown in color with no change in skin texture, is due to melanin, and on histologic examination is similar to the pigmentary lesion of neurofibromatosis (see illustrations³¹⁵). The skin pigment is often distributed in the same general area of the body as that in which the cystic bones are located. Its occurrence in children, the pigmented areas and endocrine stigmas, lack of generalized decalcification and normal blood calcium and phosphorus values serve to distinguish this disorder from hyperparathyroidism with osteitis fibrosa cystica generalisata. Thannhauser³¹³ has recently suggested, citing much evidence in support of his belief, that the pathogenesis of neurofibromatosis and that of osteitis fibrosa cystica localisata and disseminata are related. He refers to them as neurofibromatosis (Recklinghausen) and osteitis fibrosa cystica localisata et disseminata (Recklinghausen). The many similarities of the pigmentary syndromes of both conditions are strikingly emphasized in his paper.

Leschke's syndrome,³¹⁷ the association of the pigmentary syndrome of neurofibromatosis with an endocrine syndrome, is probably only a variant of neurofibromatosis. It has been especially emphasized in the German literature (see illustration³¹⁸).

The association of skin melanomatosis with melanomatosis of the central nervous system, aside from the possibility of a skin melanoma metastasizing there, has been reported^{319, 320} and is considered

*From the Evans Memorial, Massachusetts Memorial Hospitals; the Fifth and Sixth (Boston University) Medical Services, Boston City Hospital; and the Department of Medicine, Boston University School of Medicine.

†Associate professor of medicine, Boston University School of Medicine; physician-in-chief, Fifth Medical Service, Boston City Hospital, and assistant physician, Clinical Staff, Evans Memorial, Massachusetts Memorial Hospitals.

a congenital neurocutaneous syndrome and grouped with tuberous sclerosis of Bourneville and Brissand, neurofibromatosis and hemangiomas of the meninges associated with similar nevi of the skin. The pigmented spot that occasionally occurs on the back over the site of a spina bifida occulta probably also belongs in this group of pigmentation due to increased melanoblasts.

HEMOGLOBIN PIGMENTATIONS

Variations in skin color produced by changes in the amount or nature of the hemoglobin contained in the capillaries and subpapillary plexuses of the skin are far more frequent in medical practice than are the types due to deposition of an exogenous or endogenous pigment in the tissues of the skin. This review does not cover them in any detail, but the more important ones will be mentioned so that the wide range of possible skin color change will not be overlooked.

Environmental and emotional control of skin capillaries may cause a red-flushed, a pale or a cyanotic skin. Pallor due to anemia, the reddish-blue facies of polycythemia vera (see colored plate³²¹), the cherry-red color of carboxyhemoglobinemia (see colored plate³²²), the bright red color of nitric oxide-hemoglobinemia which may result from poisoning by fumes from combustion of explosives, the chocolate-blue color of methemoglobinemia (see colored illustration³²³) and the lead or mauve-blue color of sulfhemoglobinemia are striking and contrasting examples. The color of cyanosis due to increased reduced hemoglobin may vary from the deep purplish blue (see colored plate³²⁴) of strangulation to the heliotrope cyanosis (see colored plate³²⁵) noted in certain types of pneumonia. Lewis's³ colored plates for the study of cyanosis illustrate the many tones and hues that the skin color may manifest in this condition. A predominance of oxyhemoglobin in the skin color accounts for the redness of such conditions as the flushed face of alcoholism, the emotional blush, erythemas and inflammatory lesions. Hydrocyanic acid combines poorly with hemoglobin or oxyhemoglobin, but combines readily with methemoglobin to form cyanhemoglobin, which differs from ordinary hemoglobin in its bright-red color. This compound is responsible for the bright ecchymotic spots often seen in the skin of patients who have died from hydrocyanic poisoning.³²⁶ Pronounced melanin pigmentation of the skin may serve to screen out influence on skin color due to hemoglobin variations, — that is, in Negroes, — but this is not generally so marked for mucous membranes.

METALLIC PIGMENTATIONS OF THE SKIN

Hemosiderosis

"Hemosiderin" is the name applied to an iron-containing pigment that mainly occurs in the body

as a result of local or general destruction of blood and in hemochromatosis. "Hemosiderosis" is a general term used to designate the process characterized by deposition of hemosiderin pigment in the superficial corium, with resultant pigmentation. How much of the pigmentation can be directly attributed to hemosiderin deposition alone and how much to melanin production initiated through local action or through deposition of hemosiderin in the adrenal glands is not entirely clear. In some forms of hemosiderosis an accompanying melanin pigmentation — that is, hemochromatosis — is common. Hemochromatosis and a variety of hemologic disorders are the main systemic causes of hemosiderin formation. The most frequent type, however, occur on the lower legs because of a variety of combinations of local and systemic disturbance.

Hemochromatosis. Pigmentation of the skin is one of the most constant and characteristic features of hemochromatosis. Butt and Wilder³²⁷ noted its absence in only 1 of 30 cases studied by them. Case reports stressing the rarity of its absence attest to the almost constant presence of the pigmentation.^{328, 329} This may appear late in the disease, but it is often present for years and is frequently the first symptom to attract attention.³³⁰

A detailed discussion of skin pigmentation is given by Sheldon³³⁰ and Hellier.³³¹ Hemofuscin, an iron-free pigment, although usually present in hemochromatosis is not highly important in causing skin pigmentation. Melanin and hemosiderin are the two pigments concerned with the changes in color of the skin. Hemosiderin is found chiefly in the corium, mainly in the neighborhood of the sweat glands, and perhaps to some degree in the deeper epidermis.³³⁰ It is at times solely responsible for pigmentation of a bluish-black, slate or lead color, which is sometimes generalized but is always more marked on the face, the neck, the extensor surfaces of the limbs and usually the external genitalia.^{330, 331} Melanin is found in the deepest layers of epidermis and occasionally to a small degree in the chromatophores of the corium. Alone, it causes the usual brownish type of pigmentation characteristic of melanin pigmentation.

It appears from case reports that melanin tends to be the earlier type of pigmentation. This is suggested by the almost constant presence of hemosiderin in the skin in autopsy reports, whereas many biopsy studies of the pigmented skin at earlier stages reveal no hemosiderin. When both pigments are present, melanin modifies the color and blends the slate gray of hemosiderin with brown to give a bronzed appearance³³¹ (see colored plates³³²⁻³³⁵).

Hellier³³¹ records the findings of the skin histology of 57 cases from the literature and his own as follows: hemosiderin was present in 48 cases, absent in 5, and not mentioned in 4; melanin was present in 35 cases, absent in 12, and not mentioned in 10.

cases hemosiderin was present without melanin; these patients had a slate-gray or bluish color. It is evident that melanin pigmentation is far more frequent and contributes more to the skin color than is generally appreciated. The classic bronze color depends on this frequent combination of the two pigments. The early appearance in the skin of melanin pigmentation alone suggests that the mechanism is related either to hemosiderin deposition in the adrenal glands or perhaps to cortical function of some other nature.^{330, 331}

In Sheldon's³³⁰ extensive review the mucous membranes were reported as pigmented in 16.7 per cent of the cases studied — usually in the mouth and next most frequently in the conjunctivas. The pigment is apparently of the melanin type, although one report of the demonstration of hemosiderin was given.

The intensity of the pigmentation has been reported as occasionally increasing noticeably shortly before death,³³⁰ and also as diminishing rapidly when the diabetes accompanying the disorder is controlled with insulin.³³⁶ This is usually attributed to a metabolic change within the skin cells that alters its optical character rather than to dissolution or removal of the pigment.³³⁰

Skin biopsy in hemochromatosis is often poorly handled for the best results. The pigments are diffusely deposited in the skin over the entire body. One should avoid taking the skin from the legs, over pressure areas or irritated areas or from a body fold. Hemorrhagic disorders and blood dyscrasias as causes of hemosiderin formation must be excluded by appropriate hematologic studies. A request should be made for the study of melanin pigmentation as well as of stains for the iron-pigment fraction. Other aids to the diagnosis of hemochromatosis are Rous's test of the urine sediment,³³⁷ examination of sediment from ascitic fluid for iron pigment,³³⁸ the presence of insulin-resistant diabetes³³⁹ or, for that matter, any degree of diabetes in a pigmented patient or diabetes with an elevated basal metabolic rate, pigmentation in a patient with ascites, cirrhosis or an enlarged liver, Fishback's skin test³⁴⁰ and evidence of sexual hypoplasia.³⁴¹

Hemosiderosis of the lower legs. Hemosiderosis of the lower legs with skin pigmentation is frequently encountered in both general and dermatologic practice. Either gross or microscopic extravasation of red cells into the skin for long periods of time leads to deposition of hemosiderin pigment in the corium and gradually to pigmentation of the skin, usually a brownish, sepia or copper hue. It may be fairly diffuse or centered about ulcers of all types. It is oftenest seen with the stasis of varicose veins but is not uncommon in patients with other types of stasis, for example, chronic ascites.

Inflammatory and other stimulants for melanin formation are also present. Patients with this type

of leg pigmentation who have glycosuria, an enlarged liver, cirrhosis, ascites and so forth are often erroneously suspected of having hemochromatosis and a biopsy specimen of skin is taken from the pigmented area, the report of which leads to more confusion.

Supporting pressure on the tissues from shoes tends to protect the feet from the hemosiderosis. It is likely to commence near the ankle, to extend a variable distance toward the knee and to be more prominent anteriorly than posteriorly. Any hemorrhagic disorder if chronic, increased fragility of capillaries, diminished tissue elasticity of old age and so forth, if added to venous stasis, may accentuate the development of the process.

Of general medical interest is the occurrence of this type of skin pigmentation as a sequela of repeated mild trauma to the lower legs, in stasis from varicosities and probably other causes, in hemochromatosis (here diffuse over the body and not limited to the legs); about the leg ulcers in sickle-cell anemia,¹⁷⁴ congenital hemolytic jaundice,^{171, 172} in Cushing's disease,³⁷⁰ Gaucher's disease,¹⁸⁵ in perniosis,³⁴² and probably in other conditions. The occurrence of pigmentation on the lower legs, especially in a young person without varicose veins, may be a clinical finding of some significance. Of dermatologic interest are Schamberg's disease^{343, 344} (see colored plate³⁴⁵), Majocchi's disease³⁴⁴ and others.^{343, 346, 347} These disorders are listed in Table 3.

Argyria

Argyria is the pigmentation resulting from deposition of silver in the corium of the skin and mucous membranes. The monograph on argyria by

TABLE 3. *Causes of Hemosiderosis of the Lower Legs.*

CAUSES OF GENERAL MEDICAL INTEREST	CAUSES OF DERMATOLOGIC INTEREST
Repeated minor trauma	Schamberg's disease
Venous stasis of leg veins, especially from varicose veins	Majocchi's disease
Hemochromatosis	Pigmented purpuric lichenoid dermatitis
Gaucher's disease	
Cushing's syndrome	
Perniosis*	
Congenital hemolytic jaundice*	
Sickle-cell anemia*	

*Included in this tabulation on circumstantial evidence. The nature of the pigmentation is not clearly stated in the available literature.

Hill and Pillsbury³⁴⁸ based on over six hundred references attests to the world-wide interest in this subject. Any silver compound is capable of producing argyria when used for a sufficiently long period of time by any route of administration other than the intact skin. Argyria may result from the therapeutic use of silver as well as industrial exposure to it.³⁴⁹ The incidence of the condition appears to be increasing.^{348, 350} Silver is accumulated in the body over many years, and argyria develops when a sufficient amount has been deposited in the skin. The last silver preparation used before the

appearance of argyria is often erroneously blamed; if not sufficiently large in itself, it was only the amount that, added to previously stored silver, allowed the visual threshold to be reached. Silver can be demonstrated quantitatively in the skin by spectroscopic examination long before it is clinically observable.

Argyria is permanent and, other than the cosmetic disfiguration, has no effect on health. No adequate method of treatment is available, but small areas may be partially bleached.³⁵¹ Silver is deposited uniformly over all skin and mucous membrane surfaces in the corium but not in the epithelium. The areas of the body exposed to sunlight become strikingly accentuated, and such exposure should be strictly avoided by those with argyria of even minimal degree. Histologic diagnosis can readily be made from a skin biopsy.³⁵²

Argyria is clinically most pronounced on the face, hands, conjunctivas and fingernails. Because of pigment deposition in the corium, the color of argyria is usually described as slate gray, blue gray or lead, or in other words a blue varying from gray to blue (see colored illustration³⁴⁹). The ability of the pigmentation to simulate cyanosis is striking.^{348, 349} Levine and Smith³⁵³ recently reported 5 cases of argyria erroneously treated for cardiac disease because the argyria pigmentation had been mistaken for cyanosis. This has occurred in 3 patients studied at the Boston City Hospital. If the pigmentation is predominantly of a lead rather than a blue hue, the condition may be confused with melanosis or hemochromatosis.

Chrysiasis

Schmidt^{354, 355} has presented a valuable review of chrysiasis. He defines it as "a permanent pigmentation of the skin caused by the parenteral use of a gold preparation and the subsequent exposure of the skin to ultraviolet radiation, including sunlight." This potential hazard should be known to all physicians using gold. Chrysiasis is not uncommon after its excessive use.³⁵⁴ A latent period of one month to five years may elapse before the skin pigmentation makes its appearance; it then persists permanently. Lorenzen's³⁵⁴ study showed that "no patient receiving a total dose of less than 50 mg. of gold sodium thiosulfate per kilogram of body weight had definite chrysiasis and that no patient escaped having the condition if the total dose received was 150 mg. per kilogram of body weight." Cases in the earlier literature were noted after the gold therapy of tuberculosis, but gold therapy has been extensively used in arthritis in recent years, apparently without causing chrysiasis.³⁵⁶ The disease may appear only after a long latent period, so that a long follow-up is needed for one to be certain on this point.

The involved skin has been described as uniformly gray, slate gray, grayish purple, grayish blue,

bluish violet, blue green and brownish yellow. Chrysiasis appears after exposure to sunlight and is usually limited to the exposed portions of the body — the face, neck, arms, hands and sclera. The mucosa of the mouth is usually not stained. Predominant deposition in the upper corium accounts for the characteristic gray to blue hue of the skin pigmentation. Diagnosis can be made from dark-field study of histologic sections.^{348, 357} Treatment is not successful. Prophylaxis depends on minimal dosage of gold salts and avoidance of undue exposure to sunlight or ultraviolet radiation.

Bismuthia

The prolonged oral use of bismuth has been reported as rarely producing a generalized persistent skin discoloration (see colored plate³⁵⁸) resembling argyria that has been called "bismuthia." The conjunctivas and oral mucosa are pigmented. Bismuth is identified by chemical examination. The pigment granules are seen on histologic study to be evenly scattered through the corium. The rarity of this condition in spite of the common use of bismuth is worthy of emphasis. The factors essential for its production are not known. A black line of bismuth sulfide along the gums near the teeth is frequently seen in persons treated with bismuth. Tartar deposits on the teeth accentuate its formation. Pigmentation of the tongue and buccal mucosa is a warning symptom of impending stomatitis and nephritis.³⁶⁰

Wiener³⁶⁰ reported a case of bismuth pigmentation of the entire vagina in a syphilitic woman with ulcerative cervical cancer who had received bismuth therapy. This clinical syndrome appears at first glance to be analogous to the bismuth pigmentation of the gums, but may be more complex. Sulman et al.³⁶¹ treated 122 female albino rats with daily injections of bismuth and estrogenic or gonadotropic hormone preparations. Thirty to 80 per cent of the animals showed bismuth pigmentation of the vagina, but 60 control female rats treated with bismuth alone showed no blackening of the vagina. The pigmentation was believed to have been conditioned by hyperemia of the vagina from the hormone therapy, together with some unknown factor causing selective fixation of bismuth in the vagina.

Hydrargyria

Face creams containing mercury or mercury and bismuth may produce a peculiar discoloration of the skin (a brownish, gray or slate color), usually of the face and neck and limited to the areas where the material is applied, with accentuation in skin folds (see illustration³⁶²). Biopsy material shows mercurial deposits in the epithelium and corium.³⁶²⁻³⁶⁴ This type of pigmentation is purely of local origin. Goeckermann³⁶⁴ has commented on the ease with which it has been confused with pigmentations of

emic origin. The differential diagnosis of facial pigmentations is given in detail by Hollander³⁶² and others.^{359, 365}

d Pigmentation

The deposition of lead as lead sulfide within the tissue of the gums about 1 mm. from the border of the teeth, producing the so-called "lead line" or "Burtonian line" is widely recognized as one of the characteristic but not constant signs of lead poisoning. Lead does not cause pigmentation of the skin. The ashen-lead color of the face and pallor of the lips noted in lead poisoning is believed to be due not only to anemia but in addition to a possible action of lead on the skin capillaries.^{366, 367}

e Pigmentation

A permanent tattoo type of brown pigmentation of the skin may result if ferrous sulfate or ferric chloride solution along with solution of lead or aluminum acetate is used on a vesicular or open skin lesion, allowing contact of the chemical with the dermum. Pigmentation is due to dyeing of the corium with basic ferric acetate. Other agents than acetate may likewise enable iron to fix itself permanently to the protein molecule.³⁶⁹⁻³⁷⁰ This type of pigmentation is purely of local origin. In contrast to hemosiderin, metallic iron does not cause pigmentation of the skin through systemic action.

MISCELLANEOUS PIGMENTATIONS

a Porphyria

Watson³⁷¹ in reviewing the clinical features of porphyria points out that pigmentation of the skin is not uncommon in this disorder but that the nature of the pigment has not yet been determined. In congenital porphyria, he adds, uroporphyrin has been identified in the epithelial cells, where it is undoubtedly responsible, at least in part, for the marked sensitivity to light, a phenomenon that is usually absent in the intermittent acute type. In the congenital form of porphyria the teeth may be stained pink (see colored plate³⁷²).

Pigmentation of the skin in the intermittent acute types of porphyria is much more prominent on the exposed surfaces than on others; it may be patchy or diffuse, but at times covers the entire body and is bronze. Watson³⁷³ has not noted pigmentation of the mouth or other mucous membranes, a point also made by Nesbitt.³⁷⁴ Vitiligo was noted in 1 patient,³⁷¹ an observation suggesting a disturbance of melanogenesis in the skin. Whether the responsible pigment is melanin is not known. Porphobilin, a red-brown pigment occurring in porphyria, somewhat similar to urobilin but not having porphyrin characteristics, may be related to the skin color.³⁷¹ It would be quite compatible with its physical characteristics to find deposits of it in the skin.³⁷¹ Turner and Obermayer³⁷⁵ report

a case of porphyria accompanied by epidermolysis bullosa, hypertrichosis and melanosis.

Methemalbuminemia

Fairley^{169, 170} has recently given a detailed account of the blood pigment methemalbumin, first described by him in 1934. The chocolate-brown color it gives to plasma and its absorption characteristic on spectral analysis are so similar to the effects of methemoglobin that they have in the past been readily confused. It is pointed out that both methemoglobin and sulfhemoglobin are essentially confined within the red cells and that the term "methemoglobincythemia" should replace "methemoglobinemia" and "sulfhemoglobincythemia" should replace "sulfhemoglobinemia." Methemalbumin, on the other hand, is found only in the plasma. Hematin cannot exist as such in the circulating blood, and when formed combines with serum albumin to form methemalbumin. Methemalbumin is responsible for the brown color of plasma in blackwater fever and may be present in variable amounts in other hemolytic anemias. How much influence this pigment has clinically in causing changes in skin color is not clearly stated in the literature.

Malarial Pigmentation

Books on differential diagnosis commonly list chronic malaria among the disorders causing skin pigmentation. Some melanin pigmentation no doubt occurs, but the pigment problem in malaria is by no means simple. It is well known that the malarial pigment hematin is widely deposited in tissues, particularly in those of certain visceral organs. Furthermore, hemosiderin is formed.³⁷⁵ Jaundice occurs in some forms of malaria. Hemoglobinemia and methemalbuminemia occur in blackwater fever.^{169, 375} Strong's³⁷⁶ monograph on tropical medicine gives a detailed discussion of this complex subject.

Pigmentation Due to Other Medicinal Agents

Many colored chemicals, used either therapeutically or diagnostically or acting as poisons, often produce temporary skin discoloration. All physicians are familiar with some of these substances. Typical of this group are methylene blue, injectable Prontosil, Evans blue, Congo red, acriflavine, san-tonin, atabrine, dinitrophenol and many others.

Other Pigmentations

Vitiligo and gray hair. Vitiligo and canities represent diminution or absence of normal pigmentation of the skin and hair, respectively. Vitiligo stands in strong contrast to the hyperpigmentation of the skin discussed in this paper. It is beyond the scope of this review to discuss these subjects in detail. Considerable interest now centers in the possibility that the presence of gray hair is in some way related to a deficiency of one or more of the factors

of the vitamin B complex. An appraisal of the therapeutic efficacy of vitamin treatment of gray hair is not warranted at present. The status of this subject is given in two recent reviews.^{377, 378} Undoubtedly there is much to be learned about the systemic causes and associations of gray hair, as witness its occurrence in such widely separated disorders as pernicious anemia, Werner's syndrome²⁰⁸ and the Vogt-Koyanagi syndrome.³⁷⁹

It is of considerable interest that patches of vitiligo not uncommonly coexist in the very skin showing hyperpigmentation. Vitiligo occurs in Addison's disease, hyperthyroidism, scleroderma, arsenic poisoning, pernicious anemia and many of the other diseases with melanin skin pigmentation. These paradoxical combinations at present admit of no clear-cut explanation. Vitiligo may result from a variety of local skin lesions, a subject well

Roumanians, Chinese, Syrians and others. It gives an excellent description of physiologic pigmentation, which is minimal in infancy and complete by the end of the second decade. ³⁸¹ and Greenbaum³⁸¹ discuss in some detail physiologic oral pigmentation. The work of Baker,²⁰ Laidlaw³⁸⁶ and others showed that in the majority of white persons pigment cells (melanoblasts) can be demonstrated microscopically in the mucosa even if pigmentation is not grossly observable. These pigment cells are therefore subject to many of the same factors known to influence similar cells in the skin. It follows that oral pigmentation is of far more clinical significance in a person of light than in one of dark complexion. It is not itself of diagnostic value. Furthermore, many local exogenous pigmentations occur, chiefly from metals, and usually stain the gum and

TABLE 4. Conditions Governing Pigmentation of the Oral Mucous Membranes.*

USUALLY PRESENT	OCCASIONALLY PRESENT	RARELY OR NEVER PRESENT	PIGMENTATION OF MOUTH WITHOUT SKIN PIGMENTATION†‡
Pallor (anemia)	Gaucher's disease	Carotenemia	Lead (Burtonian) line
Cyanosis (reduced hemoglobin)	Niemann-Pick's disease	Sprue	Bismuth line§
Erythremia	Vagabond's disease	Hodgkin's disease	Argyria
Jaundice	Pernicious anemia†	Chrysiasis	Hydrargyria
Addison's disease	Hemochromatosis	Pellagra	Chalcosis (copper pigmentation)
Argyria	Arsenic poisoning	Porphyria	Zinc pigmentation
Acanthosis nigricans	Scleroderma		Charcoal (in tooth powder)
Lead poisoning	Tuberculosis		Smokers' patch
Bismuthia	Malaria		Tobacco chewing
Normally (darker racial groups)	Cachexia		
Methemoglobinemia	Hyperthyroidism		
Sulfhemoglobinemia			
Carboxyhemoglobinemia			

*The tabulation based on general medical literature. Sufficient data to classify every pigmentary disorder are not available.

†Frequency appears less in the current literature than in the older literature.

‡Bismuth pigmentation of skin (bismuthia) is a great rarity.

§Metals usually present a metallic sulfide line in the gums near the teeth, which is occasionally present more diffusely.

¶For further information on this group see references.³⁸¹⁻³⁸⁴

discussed in the standard textbooks on dermatology. Vitiligo also frequently occurs without any apparent local or systemic cause.

It is, also of interest that Mussio Fournier, Cervino and Conti³⁸⁰ have reported using pituitary melanophore hormone preparation for the treatment of vitiligo, apparently with some success, whether this preparation was given intradermally, locally by electrical transfer or parenterally.

Pigmentation of mucous membranes of mouth. The value and limitations of pigmentation of the mucous membranes of the mouth as a diagnostic sign of systemic disease appear to be poorly understood. Many physicians associate it exclusively with Addison's disease. The literature contains a number of excellent discussions of this subject.³⁸¹⁻³⁸⁵

Oral pigmentation (melanoplakia) is normally a racial peculiarity. Monash³⁸³ demonstrated that only 5 per cent of 200 Negroes showed no pigmented areas in the mouth. During a six-month period he noted oral pigmentation in 30 persons of various racial groups including Italians, Jews, Greeks,

near the teeth and occasionally the tissues elsewhere in the mouth. Not all mouth pigmentation are due to melanin. Furthermore, melanin pigmentation, if deep in the tissues, may look bluish and be confused with cyanosis. Diffuse oral argyria is common. Jaundice is readily detected in the mucous membranes of the mouth, as are all the hemoglobin pigments. Table 4 contains statistics based on the literature that may be of diagnostic value if interpreted in the light of the aforementioned discussion.

External pigmentation of eye. The accompanying presence, and in some cases the persistence, of pigmentation of the various external membranes of the eye—the palpebral and bulbar conjunctivas, sclera and cornea—as related to various skin pigmentations is of considerable general clinical interest and often of diagnostic aid.^{108, 183, 226, 307, 387, 388} At times the nature of the extraocular pigmentary syndrome is pathognomonic. Examination of the eye must be made in a general light, not omitting an oblique view. The use

magnifying lens is helpful. Co-operation with ophthalmologist to secure inspection with a lamp and corneal microscope may enable to detect pigmentary deposits long before they are evident in the skin, for example, in ochronosis and argyria. Observation with fluorescent light enables pigmentation not visible in ordinary light to be seen.³⁰⁷ Table 5 contains information that

TABLE 5. *Diagnostic Value of the Association of the Absence or Presence of Pigmentation of the External Portion of the Eye with Skin Pigmentation.**

PIGMENTATION OF EYE AND SKIN	PIGMENTATION OF SKIN WITHOUT PIGMENTATION OF EYE	PIGMENTATION OF EYE WITHOUT PIGMENTATION OF SKIN†
Jaundice	Carotenemia	Blue scleras of
Ochronosis	Atabrine pigmentation	osteogenesis im-
Reck's disease		perfecta
Hemochromatosis		Kayser-Fleischer ring
(less than 15 per cent)		of Wilson's disease
Argyria		Pigmentation of
Thyriasis		chromium workers
Alismuthia		Chalcosis (copper
Melanin		pigmentation)
Pigmentation‡		Siderosis bulbi
Pseudojaundice (picric		
acid pigmentation)		
Cyanosis§		
Pallor (anemia)		

*Sufficient data to classify every pigmentary disorder are not available, only the combinations found fairly consistently are listed

†See references 327, 328 for further data on these conditions

‡Melanin pigmentations of the skin are only occasionally associated with extraocular melanosis.

§Cyanosis is more difficult to detect in the conjunctiva than in the mucous membranes of the mouth.

may be of some aid in orienting the reader to the diagnostic possibilities of the associations mentioned. The lists are by no means complete, since clear-cut statements concerning extraocular pigmentation in many pigmentary disorders are not given in the available literature. It should not be overlooked that melanoblasts have been demonstrated in the conjunctival mucosa¹⁰⁹ and that in certain diseases they are potentially capable of causing a clinically detectable melanin pigmentation. It is not clear from the literature how frequently extraocular melanosis occurs in the various diseases with skin melanosis. It should not be confused with the pigmentary disturbances of the retina and choroid, for example, retinitis pigmentosa. Rarely a systemic disorder such as Addison's disease causes pigmentation of the retina that can be seen on ophthalmoscopic examination.³⁵⁹

Pigmentation of fingernails. In contrast to the observation of the mouth and eyes, that for changes in the color of the fingernails in systemic disorders with pigmentation is of limited clinical value. That the fingernails may be pigmented was well shown by Monash,³⁹⁰ who found that such pigmentation in Negroes is a normal finding of common occurrence, usually in the form of pigmented longitudinal stripes, and in darker-skinned Negroes in that of a diffuse pigmentation in addition. Pigmentation

of the fingernails may occur in white persons with disorders likely to produce marked melanosis of the skin, such as Addison's disease³⁹¹ (see illustration²⁴⁶). Mees's stripe in arsenic poisoning^{213, 392} may be simulated by other white striae^{393, 394} (see colored plate³⁹⁴). The striped area when shed can be analyzed for arsenic. Argyria causes pigmentation resembling cyanosis, but capillaroscopic examination of the nailbeds reveals a normal capillary blood flow.³⁹⁵ Gold therapy is said to pigment the nails.³⁹¹ Pigmentation of the fingernails during hyperthyroidism has been reported.³⁹⁶ The use of phenolphthalein is listed as rarely causing a bluish discoloration of the fingernails.³⁹⁷

LABORATORY DIAGNOSIS OF THE CAUSES OF SKIN PIGMENTATION

The limitations of the human eye in analyzing the causes of skin color changes should be apparent from what has been written. Spectrophotometric analysis of the skin allows recognition of both the amount and nature of the pigments present, but unfortunately the complicated technic and costly apparatus required limit its use to research studies. Under fluorescent light, some pigmentations not visible to the eye in daylight or artificial light can be readily seen (see illustration³⁰⁷). A routine history and physical examination and the ordinary laboratory work clarify the cause in most cases. The red-cell count and hemoglobin determination reveal an increase or diminution of hemoglobin in the blood. Spectroscopic examination of the blood detects methemoglobinocytopenia, sulfhemoglobinocytopenia, carboxyhemoglobinemia and methemalbuminemia. Cyanosis not due to other hemoglobin derivatives is caused by increased amounts of reduced hemoglobin. Porphyrins can be detected in the urine in porphyria by spectroscopic examination. The quantitative van den Bergh test of serum for jaundice and the Greene-Blackford test for carotenemia are highly specific. Picramic acid and atabrine can be detected chemically in the urine. Rous's test of the urine for hemochromatosis, although not entirely specific, is frequently employed. All these tests are for pigments present in the blood or urine. The Brugsch test⁴³ and the histamine wheal test for jaundice, as well as the Fishback test³⁴⁰ for hemochromatosis, are skin tests occasionally used.

Pigments deposited in the skin tissues may be studied by histologic examination of tissue obtained by biopsy. In a general hospital this method is rarely utilized to its full advantage. Requests are usually made by the physician, who understands but little of dermatology and less of the methods and limitation of histologic study of the skin. Skin biopsy specimens are often taken by a surgeon who not only has a limited knowledge of skin pigmentation but is often further handicapped by being given no specific directions concerning the most desirable

place from which to take the specimen. Unless studies are specifically requested, the pathology department is likely to fix and stain these specimens in the same manner as other types of biopsy material.

It is generally agreed by dermatopathologists that skin biopsy specimens routinely fixed in formaldehyde and stained with hematoxylin and eosin are not adequate for the study of cytology and especially for evaluation of the cause of pigmentation.³⁹⁸ Bloch's Dopa reaction to detect activity of melanoblasts,¹⁶ Masson's trichrome stain for cellular detail,³⁹⁹ silver stains to demonstrate localization and extent of melanin pigmentation, Osborne's method for demonstrating arsenic crystals in the skin,²¹⁷ special fixatives for skin tissue, dark-field examination of sections lightly stained with polychrome methylene blue, which enables one to visualize the various metallic pigment granules, as in argyria and chrysiasis, as refractile granules and excludes the nonrefractile granules of melanin and hemosiderin, spectrographic examination of biopsy tissue for detection of metallic pigments,³⁵⁰ Mallory's potassium ferrocyanide method for staining hemosiderin and Mallory's fuchsin stain for hemofuscin are typical of the many technical approaches available to the skilled dermatopathologist. It is apparent from this review that the cause of many types of melanin pigmentation cannot be determined histologically and that diagnosis depends chiefly on routine clinical and indicated laboratory procedures.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND SIXTY-THIRD ANNIVERSARY

May 22, 23 and 24, 1944

THE one hundred and sixty-third anniversary of the Massachusetts Medical Society was observed in Boston on Monday, Tuesday and Wednesday, May 22, 23, and 24, 1944, at the Hotel Statler. Fourteen hundred and forty physicians were registered.

MONDAY, MAY 22

The supervising censors met at 5:00 p.m. in Parlor D.

The Cotting Supper was served to 197 councilors in Parlors A and B. The annual meeting of the Council was held in the Georgian Room, at 7:00 p.m. There were 218 councilors in attendance.

TUESDAY, MAY 23

The first general session was presided over by Dr. George L. Schadt and Dr. G. Lynde Gately, acting as chairman and co-chairman, respectively. The attendance was as high as 650.

This session took the form of a symposium on war injuries.

The one hundred and sixty-third annual meeting of the Society was held at 11:00 a.m. in the Georgian Room. Dr. Roger I. Lee presided. The attendance was 450.

Dr. Lee spoke at length on the state of the Society. The annual oration entitled "A Toxic Factor in

Experimental Traumatic Shock," was delivered by Dr. Joseph C. Aub.

During the course of the meeting the President presented Dr. George Mathews, of Providence, delegate from the Rhode Island Medical Society, and Dr. G. Gardiner Russell, of Hartford, delegate from the Connecticut State Medical Society. They responded fittingly.

The annual luncheon was served in Parlors A, B and C to 156 fellows.

A clinical meeting was held in the Georgian Room from 2:00 to 4:00 p.m., under the chairmanship and co-chairmanship of Dr. Dwight O'Hara and Dr. Clifton T. Perkins, respectively. The attendance was 600.

The Shattuck Lecture was delivered at 4:00 p.m. by Dr. Alfred Blalock, of Baltimore, Maryland. Dr. Blalock's subject was "A Consideration of Recent Advances in Surgery." (This lecture will appear in the *New England Journal of Medicine*, issues of August 17 and 24.)

The annual dinner was held in the Georgian Room at 7:00 p.m. with 492 in attendance. This dinner was graced by the presence of the Honorable Leverett Saltonstall, Governor of Massachusetts. William Cunningham, of the *Boston Herald*, was the principal speaker.

WEDNESDAY, MAY 24

There was a general clinical meeting in the Georgian Room from 9:00 a.m. to noon under the chairmanship and co-chairmanship of Dr. Charles F. Wilinsky and Dr. Leroy E. Parkins, respectively. The attendance was 600.

From 12:00 noon until 2:00 p.m. a series of section meetings and luncheons was held.

The Section of Medicine, under the chairmanship of Dr. George D. Henderson, met in Parlor B. Because of the numbers attending, it was adjourned to the Georgian Room. Sixty-two sat down for luncheon, and approximately 300 attended the clinical meeting afterward.

The Section of Surgery, under the chairmanship of Dr. Howard M. Clute, met in Parlor C. The attendance was 65.

The Section of Pediatrics, under the chairmanship of Dr. Leroy T. Stokes, met at The Junior League, Zero Marlboro Street. The attendance was 54.

The Section of Obstetrics and Gynecology met in Parlor A, under the chairmanship of Dr. Christopher J. Duncan. The attendance was 62.

The Section of Radiology met in Room 716 W, under the chairmanship of Dr. Stanley A. Wilson. The attendance was 25.

The Section of Physiotherapy met in Parlor E, under the chairmanship of Dr. Wilmot L. Marden. The attendance was 13.

The Section of Dermatology and Syphilology met in the Hancock Room, under the chairmanship of Dr. John G. Downing. The attendance was 35.

The New England Society of Anesthesiology met in Parlor D. The attendance was 32.

From 2:00 to 5:00 p.m. a general clinical meeting was held in the Georgian Room under the chairmanship and co-chairmanship of Dr. Daniel B. Reardon and Dr. Vlado A. Getting, respectively. The attendance varied from 450 to 600.

There were eighteen scientific and seventy-six technical exhibits.

The motion pictures, as usual, attracted a large number.

The official list of officers, standing and special committees, councilors, censors, admissions, deaths and so forth are appended.

MICHAEL A. TIGHE, *Secretary*

ANNUAL MEETING OF THE SOCIETY

The one hundred and sixty-third annual meeting of the Massachusetts Medical Society was called to order by the president, Dr. Roger I. Lee, in the Georgian Room of the Hotel Statler, Boston, at 11:00 a.m., May 23, 1944. There were approximately 450 fellows present.

The Secretary offered the record of the last annual meeting as published in the *New England*

Journal of Medicine, issue of July 22, 1943. There being no objection, this report was declared accepted by the chair.

Dr. Lee presented Dr. George Mathews, of Providence, representative of the Rhode Island Medical Society. Dr. Mathews brought the greetings of the society.

Dr. G. Gardiner Russell, of Hartford, Connecticut, was introduced and brought the greetings of the Connecticut State Medical Society.

The Secretary announced that the membership of the Massachusetts Medical Society, as of May 23, 1943, was 5753, and as of May 23, 1944, 5778. He said that 104 fellows had died, 11 had resigned and 1 had been deprived of membership during this interval. He added that 129 new fellows had been created and that 12 had been reinstated during this period. The net gain in membership, he said, was 23.

The following amendments to the by-laws were read by Dr. Lee:

Chapter IV, Section 4, of the by-laws of the Massachusetts Medical Society is amended by striking out the word "stated" appearing in the first line and inserting in its place the word "annual," by deleting the words "in October" appearing in the second line, by striking out the word "stated" in next to the last line and inserting in its place the word "annual" and by deleting in the last line the words "in February."

The amended section reads as follows:

Section 4. The Council shall elect at the annual meeting, on nomination by the President or from the floor, the Auditing Committee, composed of two fellows who are not councilors.

This committee following the close of the fiscal year, shall require by a certified public accountant an examination of the assets and securities of the Society in the custody of the Treasurer, and of the Treasurer's books and accounts.

This committee shall verify the accountant's examination and report its findings at the annual meeting of the Council.

Chapter VI, Section 5, of the by-laws of the Massachusetts Medical Society is amended by striking out the word "February," as it appears in the fifth line of page 21, and inserting in its place the word "annual."

This amended paragraph reads as follows:

He [the Treasurer] shall render to the Council at its annual meeting a full written report of the assets and liabilities on December 31 of the previous year, and also of the financial transactions of the Society during that year.

Dr. Lee said that the purpose of these changes was to allow more time for the auditors to do the job assigned them under the by-laws. He added that they had been favorably acted upon by the Council on May 24, 1943.

Dr. Frank R. Ober, Suffolk, moved the adoption of these two amendments. This motion was seconded by Dr. Clarence E. Burt, Bristol South, and it was so ordered by vote of the members.

Dr. Lee called on Dr. William H. Robey, Suffolk. He presented resolutions on the death of Dr. Charles S. Butler, former treasurer of the Massachusetts Medical Society. These resolutions appear on

records of the meeting of the Council held on 22, 1944.

r. Lee made an urgent plea to the district secretaries to send to Dr. Tighe the names of all physicians who had entered the armed services from their respective districts.

r. Lee called on the vice-president, Dr. Daniel Reardon, Norfolk South, to assume the chair. So doing, Dr. Reardon spoke as follows:

As your vice-president, it has been my privilege and pleasure for the past year to work with our president. I have found him an untiring, zealous and hard-working individual. He has not alone confined his time and efforts to the welfare of the Massachusetts Medical Society, but as you well know, is chairman of the Board of Trustees of the American Medical Association. To both these offices he has given time and efforts for the welfare of the medical profession in general.

It is now my distinct honor and pleasure to give you Dr. Er I. Lee, president of the Massachusetts Medical Society, who will report on the state of the Society.

Dr. Lee responded as follows:

It is a happy custom that the president of the Massachusetts Medical Society reports on the affairs of the Society at the annual meeting.

Your present incumbent finds great pleasure in making his report. Any report at this time, however, is made under the shadow of a grim catastrophe that has enveloped the entire world. It has dislocated all our lives. It has dominated all our thoughts. Of necessity, winning the war is the sole objective of all of us. We that are here are under orders if in uniform, under sentence if in civilian clothes. Perhaps a third of the fellows of this society are in uniform, and before long, as the war continues and as recent graduates go into the armed services, approximately half the active physicians of the Commonwealth will be in uniform. It is, I believe, an extraordinary tribute to the unwavering loyalty and the altruistic idealism of the medical profession that no attempt has been made to capitalize on the pressing necessity for doctors in the armed forces or on the resulting shortage of doctors on the home front. There are no doctors' blocs seeking special class legislation. There are no doctors' strikes. There are no doctor profiteers. This is no doctor "black market." And I desire to pay tribute to the wives and families of the doctors in the service. Doctors volunteer. There has been no drafting of doctors, unless one means that a man's conscience drafted him. Doctors volunteered for their soldiers' pay, not for "cost plus" and not for war workers' pay, and their wives make what shift they can. And when these men come back, let these sacrifices be not forgotten.

And in passing may I give a bit of tribute to the wives of the doctors who stayed at home! They have done double duty, quite unheralded and quite unsung. And most of the doctors' patients have, in this trying situation, been understanding and co-operative, and have cheerfully foregone on many occasions the comfort of the doctor's visit, if in his judgment a visit was not absolutely necessary.

The Massachusetts Medical Society operates through committees, which report to the Council. Four of these committees are composed of one man from each district society, elected by the district society. These are the Nominating Committee, although technically not a committee, the Committee on Public Relations, the Executive Committee and the Committee on Legislation. The nominating councilors from each district have the sole function of nominating the officers of the Society. The Committee on Public Relations is perhaps a dozen years old. This committee has been so strikingly useful along the lines of its designation that two quite new committees — the Executive Committee and the Committee on Legislation — have been set up along similar but not identical lines for their particular purposes. The president of the Society, who is an *ex-officio* member of all committees, is

named as the chairman of the Committee on Public Relations and of the Executive Committee. It is not my purpose to repeat the story of the activities of the various committees; it is rather to discuss the functioning of the committee mechanism of the Society, inasmuch as the Society operates through committees reporting to the Council.

The Executive Committee was designed for two purposes: to free the Council from considerable detail and to provide a group, informed before the Council meeting, concerning certain committee reports and other items of a complex nature. Although there has been some confusion about the extent of the authority of the Executive Committee, it is my considered opinion that this committee, which has worked very diligently, has contributed much to the thorough consideration of problems so that the Council might act wisely. It is, I believe, of great benefit to the Society that free preliminary discussion of certain questions can take place in a large representative committee like the Executive Committee, and indeed, certain problems are gone over by the Committee on Public Relations before consideration by the Executive Committee.

These four committees, excluding the *ex-officio* members, are composed of seventy-two men. Naturally some of these are duplicates. On the other hand, there are alternate members of the Executive Committee. And this number refers only to four committees, all elected by the member districts.

Most of the committees of the Society, whether standing or temporary, are small. The ordinary procedure is that the president nominates and the Council elects. The Council may also nominate. Most committees consist of five members. But there are larger committees, notably a committee of seventeen, appointed to consider a loan fund for returning medical officers of the Society. There are around 250 fellows serving on all these committees. The majority of the members of the committees are members of the Council. The chairmen of the standing committees are *ipso facto* members of the Council. The Council numbers at this time 328. The number of fellows in the Society is about 5778.

Your president has always believed that service on the committees of the Society was both an obligation and an opportunity and should be freely shared by the fellows and that committee membership should be frequently changed. He also has strongly believed in the liberal mixture of young and old in committees. Alas for his theories. The war took off the younger men. Older men, familiar with certain committee duties, could carry on effectively with a minimum of effort. So, very regretfully, committees were frozen. But when the war is over and the fellows come back, I want this to be a public record of what one president feels regarding committee changes. I should like also to suggest a slower pace of change in some of the committees, such as the Committee on Ethics and Discipline and the Committee on Finance. I believe, too, that this should also apply to the delegates to the House of Delegates of the American Medical Association. I do not believe, however, that any committee should be regarded or regard itself as fixed.

Each of the Society's committees has made a report to the Council. These reports will be printed in the *Journal* in the near future and therefore will not be considered here.

Reports may not be very revealing. The Committee on Ethics and Discipline has a talent that approaches genius in laconic statement. Its activities are mostly confidential. The time spent by this committee is enormous. The good to the Society is incalculable.

A recent committee that has labored quietly but effectively is the Medical Advisory Committee to the Regional OPA. No fire alarms, no sirens, but some hefty spade work and a lot of sweat, and a good crop at the end. Washington says it is the best advisory committee in the country.

During this session, we have had frequent cause to be grateful to the Committee on Arrangements. Dr. Gordon Morrison reluctantly consented to remain on the job again this year. He and his hard-working committee have done a grand job. What does not appear on the surface is the liaison that Dr. Morrison has maintained between his

committee and the committees of other organizations on war meetings.

I saw Dr. Walter P. Bowers the other evening in Worcester. He said to me, "Now, don't you ever forget that I picked out Nye as editor of the *Journal*." I had thought that the Committee on Publications had picked Nye. Bill Breed claims that he discovered Nye. Under the ownership of the Massachusetts Medical Society, the *Journal* (by which I mean, of course, the *New England Journal of Medicine*) has had but two editors — Dr. Bowers and Dr. Nye. The Committee on Publications selects the Shattuck Lecturer and gives some heed to the publication of the *Directory*, and ostensibly to the *Journal*. I have been a member of that committee with Dr. Bowers as editor and with Dr. Nye as editor. I seem to recall that I announced to the Council the appointment of Dr. Nye. But, in any event, the *Journal* has prospered wonderfully in these war times. As you know, fellows in the armed forces are excused from dues, including subscription to the *Journal*. Some of us thought that, with diminished subscriptions, paper shortage and inability to take advertising, the Society might be in for a considerable loss in the *Journal* account. But, at the moment, the circulation is increasing. As a humble contributor, I can testify that requests for reprints come from nearly every state in the Union. You have every reason to be proud of the *Journal*, the editor, the editor emeritus and the Committee on Publications.

The financial status of the Society seems excellent. The new treasurer, Dr. Hubbard, has given generously of his time and energy. There is now set up a system of expert advice on securities and of modern accounting.

The additional space for the officers of the Society has permitted a considerably increased volume of work of the Society to be carried on smoothly. For example, there are sometimes as many as four committees of the Society meeting at once. Wednesday seems to be the day that the doctor takes a busman's holiday and goes to 8 Fenway, Boston, for a committee meeting of the Massachusetts Medical Society.

As you may know, plans are already under active discussion to establish an information bureau at the Society's headquarters.

As a part of his duties, the president has the privilege of visiting the district societies. This was indeed a pleasure, and it is a matter of deep regret that it was not possible to visit all the district societies. Despite the handicaps and obstacles of wartime conditions, the district societies have been able to continue to hold interesting meetings with good attendance.

Under the authority of the Executive Committee, which was subsequently approved by the Council, a committee from the Society met several times with representatives of the other New England State medical societies for discussion of legislative matters. This idea did not originate in this state. It seems to be generally true, if the New England states are a criterion, that doctors are largely uninformed concerning possible legislation involving the practice of medicine. Being uninformed the profession is often unable to bring to any discussion the benefits of its experience. Then, too, the uninformed are frequently led into unwise, irrelevant and perhaps inaccurate remarks, which are not helpful to orderly discussion. It would seem the plain duty of every member of the profession to acquaint himself fully with the various and sundry legislative proposals; he should study these proposals in the light of his own knowledge of the facts. Some of these problems are today as unanswerable as the cure of cancer or the prevention of the common cold.

Doctors are citizens and as such are entitled to political beliefs and political affiliations. But in the discussion of medical service to the people, political beliefs and political affiliation have no place. So long as the Massachusetts Medical Society is recognized as unselfish and altruistic, just so long can it expect to have its voice listened to with respect.

It is pleasant to record improvement in the relations between the Society and the regularly instituted legislative, executive and health authorities on Beacon Hill. The medical profession has no selfish interest of its own

to further. It does have a wealth of experience and knowledge that should be made available for the better of the public. The past year promises to be epochal in the standards of medical practice in Massachusetts, and if nothing unforeseen happens, the year 1944 will define the Commonwealth of Massachusetts from its unenviable position of being the dumping ground of gradedly actual, nominal or what you will, of unapproved medical schools. There is now an excellent Board of Registration in Medicine. All this comes as the result of years of effort to secure a good medical-practice Act, which is now law in Massachusetts. In this state, medical standards have suffered grievously because of excessive lay domination over the medical profession. In a recent address at the one hundred and fiftieth anniversary of the Worcester District Medical Society, I took occasion to point out that lay thought and lay influence had controlled the medical profession from the days of the medicine man to the present day. The best medical school in the country, the best hospital in the country or the best and most progressive medical society in the country does not set medical standards; but legislatures do. I am far from advocating unrestricted medical control. I admit that penicillin is a product of war conditions and that it is doubtful how penicillin would have been developed without the war. One seemingly cannot have penicillin without the war. But my sole point is that doctors do not have sufficient voice in the determination of many medical problems, particularly that concerning the standards of medical practice.

There are many fellows of the Society who have made the past year a pleasant one for the outgoing president. There is one person, not a fellow, to whom I have been indebted on many occasions for never-failing courteous co-operation, our executive secretary, Bob Boyd. And there is one fellow, who is in one person a seeing eye, a watchdog, a life-saving St. Bernard, and man's and president's best friend — the secretary of the Society, Mike Tighe.

(Dr. Lee's address, which showed not only intimate knowledge of the Society in all its affairs but likewise a very human understanding of its problems with which the war has confronted its members, was greeted with loud applause.)

Dr. Lee resumed the chair and introduced the new officers:

President: Elmer S. Bagnall, Essex North
Vice-president: Sumner H. Remick, Middlesex South
President-elect: Reginald Fitz, Suffolk
Secretary: Michael A. Tighe, Middlesex North
Treasurer: Eliot Hubbard, Jr., Middlesex South
Assistant treasurer: Norman A. Welch, Norfolk
Orator: Frank H. Lahey, Suffolk

All responded fittingly.

The President expressed his pleasure in presenting the distinguished orator, Dr. Joseph C. Aub, Boston, whose subject was "A Toxic Factor Experimental Traumatic Shock." (At the close of his oration Dr. Aub was loudly applauded. His oration will appear in the *New England Journal of Medicine*, issue of July 20, 1944.)

Dr. Reardon moved that the meeting adjourn. This motion was seconded by a member, and it was so voted.

Dr. Lee declared the one hundred and sixty-third annual meeting of the Massachusetts Medical Society adjourned at 12:20 p.m.

MICHAEL A. TIGHE, Secretary

APPENDIX

ADMISSIONS RECORDED FROM MAY 25, 1943, TO MAY 23, 1944

YEAR OF ADMISSION	NAME AND RESIDENCE	MEDICAL SCHOOL
1944	Alba, Anthony, Dorchester	Tufts
1943	Alpert, David Robert, Allston	Tufts
1943	*Alifano, John James, Springfield	Middlesex
1943	Anderson, Donald Grigg, Boston	Columbia University
1943	Anderson, Dorothy Sperling, Newton Lower Falls	Boston University
1944	Anderson, Erna Goettsch, Boston	Columbia University
1943	*Annis, Israel Alan, Auburndale	Middlesex
1943	Armstrong, Sinclair Howard, Jr., Boston	Harvard
1944	*Avallone, Louis John, Somerville	Middlesex
1943	Baker, Joseph Michael, Springfield	University of Vermont
1944	Bandeian, John Jacob, Bridgewater	Tufts
1943	Barry, Herbert, Jr., Cambridge	Tufts
1944	Beals, Lester H., Mount Hermon	University of Michigan
1944	Belin, Harry, Middleton	Tufts
1943	*Berman, Leo, Brookline	Basel University
1944	Blackmer, Lewis Dwight, Quincy	Tufts
1944	Blodgett, James Bishop, Brookline	Harvard
1943	Boone, Edward William, Boston	Harvard
1943	Booth, Marion Frances, Northampton	University of Nebraska
1943	Boynton, Willard Harold, East Boston	Tufts
1944	Bruno, Francis Ernest, Quincy	Tufts
1943	Bryan, Charles Silas, Jr., Cambridge	Harvard
1943	*Butts, Vincent, East Boston	College of Physicians and Surgeons, Boston
1944	Cahill, George Byron, Boston	University of Minnesota
1944	Carroll, Robert Ernst, Boston	Yale
1944	Chapman, William Phalen, Boston	McGill
1943	*Chase, Frank Hills, Stoneham	Bellevue Hospital Medical College
1944	*Chesnow, Albert, Great Barrington	Middlesex
1944	*Ciampa, Frank, Somerville	University of Naples
1943	*Civen, Eva, Dorchester	Middlesex
1944	Congdon, Frederick Richard, Pittsfield	Tufts
1943	Davidson, George Davis, Quincy	Boston University
1944	*Davis, Robert Armstrong, Wareham	Mid-West Medical College
1943	Dopkeen, Saul Kahn	Boston University
1944	*Drury, George Eliot, Malden	College of Physicians and Surgeons, Boston
1944	*Ehrentheil, Otto Felix, Brighton	University of Vienna
1943	*Ehrlich, Robert, Newton Centre	Middlesex
1943	Engleman, Clarence Clarke, Brookline	Western Reserve
1943	Ewing, Edward Hiltz, Stoughton	College of Physicians and Surgeons, Baltimore
1943	Fell, James Edward, Fall River	Tufts
1944	Finch, Clement Alfred, Boston	University of Rochester
1943	Floyd, Louis Carl, Brookline	University of Texas
1943	Flynn, James Lawrence, Boston	Georgetown
1943	Flynn, John F., Pittsfield	Washington University
1943	*Friedman, Sidney, Brookline	Middlesex
1943	Garrett, John William Douglas, Boston	University of Toronto
1943	Goeringer, Claire Ferdinand, Fort Devens	Johns Hopkins
1943	Hall, Albert Eden, Worcester	Long Island
1944	Halter, Paul Edmund, Boston	Western Reserve
1944	Heerdegen, Dorothy Kathryn, Jamaica Plain	Ohio State University
1944	Heimlich, Fred, Brookline	Tufts
1943	Hemenway, Ruth Victoria, Williamsburg	Tufts
1943	*Hite, Jacob William, Boston	Middlesex
1943	*Hochman, George Victor, Sharon	Middlesex
1944	Holt, William Leland, Amherst	Harvard
1943	Howard, Rutledge William, Boston	Harvard
1944	Howe, Chester W., Brighton	Tufts
1943	Hudson, Henry Alfred, Marblehead	Tufts
1943	*Johnson, Daniel Philip, Melrose	University of Lausanne
1943	Kasdon, Solomon Charles, Boston	Yale
1944	Katz, Harvey Warren, Everett	Tufts
1943	*Kay, Stephen Benjamin, Fitchburg	Middlesex
1944	Kenney, Francis R., West Newton	Boston University
1944	Landis, Eugene Markley, Chestnut Hill	University of Pennsylvania
1943	Leighton, Herbert Towle, Brookline	Harvard
1944	Le Vine, Bernard Elliot, Roxbury	Tufts
1944	Levine, Irving Maxwell, Dorchester	Tufts
1943	*Levy, David Abraham, Mattapan	Middlesex
1944	Lincoln, James Rufus, Wareham	Harvard
1944	Lockhart, Arthur John, Chestnut Hill	Columbia University
1943	Lodge, Edmund Anderson, Gloucester	University of Kansas
1943	Lynam, Patrick Joseph, Malden	Tufts
1943	*Magendantz, Heinz Herbert, Newton Highlands	University of Cologne
1944	*Makofski, Anthony B., Northampton	Kansas City University of Physicians and Surgeons
1944	*Marks, Abraham S., Malden	Middlesex

1943	McCarty, William Charles, Cambridge	Harvard
1943	McGillicuddy, John Joseph, Brighton	Yale
1944	McLaughlin, James Alphonsus, Ocean Bluff	Tufts
1943	McNulty, John Joseph, Roslindale	Tufts
1943	Meissner, William Avison, Brookline	University of Oregon
1944	Melcher, Margaret S., Northampton	Stanford
1943	*Michalski, Kasimir Stanislaw, Worcester	Middlesex
1943	Miller, Daniel, Boston	Tufts
1943	Miller, George Francis, Dorchester	Harvard
1943	*Minsky, Joseph William, West Boylston	Mid-West Medical College
1943	Money, Isabel Stirling, Mattapan	Boston University
1944	Moore, Francis Daniels, Brookline	Harvard
1944	Moss, Robert Elmer, Boston	Boston University
1943	Murphy, Albert Summers, Waban	Harvard
1943	Murphy, John Anthony, Boston	Tufts
1944	Murray, Jean, Boston	Johns Hopkins
1944	Myers, Robert Samuel, Brookline	Harvard
1944	*Neustadt, Else, Westwood	University of Leipzig
1944	*Neustadt, Rudolph, Westwood	University of Leipzig
1943	Nevin, Robert Williston, Vineyard Haven	University of Vermont
1944	O'Keeffe, James Vincent, Lynn	Harvard
1944	Ostrov, Norman N., Dorchester	Tufts
1943	Parker, Arthur Seymour, Jr., Brookline	Georgetown
1943	Parrish, Carroll Ernest, Melrose	College of Medical Evangelists
1944	Porter, Charles Talbot, Pepperell	Harvard
1943	*Portner, Irwin Isaac, Brighton	Middlesex
1943	Prince, Anna Agassiz, South Hamilton	Columbia University
1944	Provenzano, R. William, Jamaica Plain	Tufts
1944	Quinby, John Thayer, Brookline	Harvard
1943	Rice, John Dexter, Shrewsbury	Tufts
1944	Robinson, Hugh Laughlin, West Newton	Harvard
1943	Rogers, Lois Knight, Concord	Yale
1944	Rooney, John James, Waban	Columbia University
1944	*Rosenthal, Myer, Mattapan	Middlesex
1944	Saunders, Allen Irving, Roxbury	Tufts
1943	Shapiro, Robert Rubin, Brookline	Harvard
1944	*Shepard, Herbert Norman, Allston	Middlesex
1944	Sheridan, Edward Paul, Boston	Northwestern University
1944	Silverstein, Maurice L., Dorchester	Boston University
1943	Stearns, Samuel, Dorchester	University of Michigan
1944	Stratton, Harold Linson, Worcester	Tufts
1944	Taylor, Lois Ellene, Belchertown	University of Vermont
1944	Thomson, Robert Strachan, Walpole	Harvard
1944	Trafton, Howard Munro, Hyde Park	Boston University
1944	Tucker, Arthur Wallace, Jr., Needham	Harvard
1944	Tyson, Dudley Ball, Boston	Tufts
1944	*Valicenti, Peter Roger, Rockland	Middlesex
1943	Van Dyke, Wilhelmina Marie, East Milton	University of Michigan
1943	Varnerin, Emma Mary, Roxbury	Boston University
1943	*Vilker, Arthur Hyman, Revere	Middlesex
1944	Votta, Ipolidi John, Boston	Boston University
1943	Waldman, J. Edward, Malden	Tufts
1943	*Werby, Isidore, Brighton	Middlesex
1944	Zonderman, Bernard, Revere	Boston University

Total 129

*The candidate after a personal interview, was approved by the Committee on Membership and permitted to take an examination before a board of censors.

DEATHS REPORTED FROM MAY 23, 1943, TO MAY 23, 1944

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1910	†Abbe, Elizabeth Morrison	Roxbury	January 18, 1943	65
1900	†Alfred, James	Brockton	June 12, 1943	69
1883	†Atwood, Charles Augustus	Taunton	October 10, 1943	81
1939	Barrett, James Aloysius	New Bedford	April 28, 1944	55
1941	Barry, Thomas A.	"In the service of his country"	August 4, 1943	34
1914	Bell, Clarence John	Wellesley	June 6, 1943	67
1890	†Blake, John Bapst	Brattleboro, Vermont	August 17, 1943	77
1912	Brady, William Francis	St. Petersburg, Florida	February 28, 1944	53
1887	†Brennan, John Joseph	Worcester	August 26, 1943	79
1908	Broderick, Francis Patrick	Jamaica Plain	February 26, 1943	67
1899	Buehler, George Van Buskirk	Bedford	November 19, 1943	66
1921	Campbell, Charles Macfie	Cambridge	August 7, 1943	70
1898	Carden, Charles James	Tewksbury	July 4, 1943	60
1934	Chase, Lawrence Milton	Carver	February 8, 1944	70
1915	Clarke, Willis Earl	West Somerville	February 23, 1944	55

5	Cochran, John Joseph	Natick	May 1, 1944	47
11	†Colburn, Frederick Wilkinson	Boston	April 9, 1944	73
25	Connor, Thomas John	Arlington	July 16, 1943	51
37	Coriat, Isador Henry	Boston	May 26, 1943	67
95	Coues, William Pearce	Brookline	January 13, 1944	71
27	Cronin, Edward Joseph	Brighton	February 11, 1944	46
19	Curran, Louis Frederic	Dorchester	July 22, 1943	57
11	Cushman, Howard Lewis	Methuen	November 3, 1943	57
07	Dascombe, Otho Lee	Waltham	September 26, 1943	63
00	†Daudelin, Simeon Alphonse	Montreal, Canada	August 28, 1943	73
36	David, Ernest Joseph	Lowell	July 11, 1943	59
03	Donaldson, James Frank	Middleton	March 10, 1944	66
36	Dore, Rev. Francis James (Honorary Fellow)	Chestnut Hill	February 28, 1944	67
397	Egan, John Joseph	Gloucester	January 22, 1944	73
303	Elliott, Alfred	Middleboro	March 1, 1943	71
393	†Emerson, Francis Patten	Franklin	January 19, 1944	81
338	Faillace, Gaetano	Brookline	February 19, 1944	71
338	Flanagan, Lt. James Edward (MC), U.S.N.R.	"Reported missing in action"	January 2, 1944	31
884	Foster, Charles Chauncy	Cambridge	December 2, 1943	85
911	Frank, Morris	Roxbury	June 17, 1943	56
884	†Gage, James Arthur	Lowell	November 29, 1943	85
908	Geary, Cornelius Edward	Fitchburg	December 6, 1943	63
927				
896				
913	Gerstein, Maurice	Brookline	July 13, 1943	73
941				
919	Gillespie, Norman Wilkinson	Dorchester	April 28, 1944	55
924	Givan, Lt. Comdr. James Alexander (MC), U.S.N.R.	Norfolk, Virginia	November 14, 1943	43
1934	†Gleason, Edward Francis	Hyannis	April 9, 1944	75
1933	Graves, Lt. Comdr. Sidney Chase (MC), U.S.N.R.	"Somewhere in the Pacific"	Unknown	43
1910	Hallisey, Joseph Edward	Boston	November 18, 1943	61
1923	Halloran, Col. Roy Dennis, M.C., A.U.S.	Washington, D. C.	November 10, 1943	49
1900	Hart, Henry Brown	Sarasota, Florida	July 13, 1943	72
1906	Hartman, Gustave	Lynn	August 1, 1943	66
1902	Hartwell, Harry Fairbanks	Weston	December 7, 1943	70
1907	Hatch, Ralph Augustus	Brookline	April 1, 1944	62
1885	Howard, Margaret Emily Pagelsen	Reading	March 1, 1944	84
1904	Howe, Harry Newell	Greenfield	May 11, 1944	72
1897	†Jackson, Alton Atwell	Everett	July 25, 1943	89
1911	Jacques, J. Hector	Fitchburg	April 15, 1944	68
1905	Kennedy, Edward Anthony	Pittsfield	December 14, 1943	63
1909	Kennison, Fred Marshman	Boston	July 31, 1943	80
1905	Kent, Ralph Porter	Oak Bluffs	August 5, 1943	63
1898	Kite, Walter Chester	Milton	February 5, 1944	79
1899	†Laighton, Florence Marion	New York City	January 15, 1943	72
1920	Laserte, Charles John	Leominster	April 14, 1944	62
1912	Leland, George Adams, Jr.	Brookline	September 22, 1943	57
1903	Lemaire, Willard Wallace	Worcester	December 27, 1943	64
1937	Lodge, Athens Vallette	Brewster	November 18, 1943	71
1940	Lowenthal, Karl	Fall River	January 16, 1944	51
1902	Lowney, John Francis	Fall River	February 19, 1944	74
1908	Mannix, Louis Edward	Springfield	March 11, 1944	59
1914	Mason, Broadstreet Henry	West Hartford, Connecticut	January 1, 1942	60
1902	Mayhew, Orland Smith	Vineyard Haven	February 26, 1944	66
1921	McAuslan, James Lewis	North Grafton	March 22, 1944	69
1936	Merchant, Raymond Francis	Vineyard Haven	June 7, 1943	41
1936	Merrick, Frank Humphrey	Dorchester	January 17, 1944	37
1928	Miller, Howard Stephen	Taunton	September 6, 1943	55
1911				
1939	†O'Brien, John Francis	Fall River	June 11, 1943	57
1928	Palmer, Anna Chipman	Brookline	February 10, 1944	86
1887	†Parks, Silas Henry	Great Barrington	November 7, 1943	82
1927	Parlow, George Gibson	Wareham	April 20, 1944	74
1911	Penny, Mary McDermott	Saugus	April 17, 1944	72
1914	Percy, Karlton Goodsell	Brookline	November 15, 1943	57
1898	Perley, Roscoe Damon	Melrose	January 21, 1944	79
1932	Phillips, Major Robert Titus, M.C., A.U.S.	Philippines	Unknown	41
1904	Pote, Leonard Holden	Somerville	December 3, 1943	69
1889	†Pothier, Joseph Charles	New Bedford	December 1, 1943	78
1923	Rich, Herbert Lowell	Attleboro	January 23, 1944	78
1908	Richardson, Edward Peirson	Brookline	January 26, 1944	62
1898	†Richmond, Simon	Roxbury	February 5, 1943	70
1907	Riley, Charles Allen	Chestnut Hill	January 30, 1944	62
1929	Seed, Raymond Charles	Lawrence	June 6, 1943	45
1920	Senecal, Raymond Ernest	New Bedford	August 24, 1943	51
1921				
1943	Silberg, Morris Abraham	Roxbury	November 20, 1943	49
1897				
1919	†Spalding, Fred Maurice	Brookline	January 24, 1944	73
1925	Spellissy, Frank Thomas	Marlboro	February 4, 1944	48
1896	Stein, Albert	Thompsonville, Connecticut	December 5, 1942	49
1920	Stetson, Halbert Greenleaf	Greenfield	September 15, 1943	75
1920	Stickney, Robert Cole	Beverly	September 7, 1943	50

1905	Stone, Ralph Edgerton	Beverly	March 22, 1944
1907	†Sullivan, John Thomas, Jr.	Dorchester	December 10, 1943
1925	†Thompson, Clara Louise	Boston	September 16, 1943
1882	†Tilton, Josiah Odin	Lexington	December 2, 1943
1914	Varney, Elton Murray	Peabody	March 11, 1944
1899	Washburn, Frank Hall	Holden	November 10, 1943
1909	Wentworth, Mark Hunking	Concord	May 15, 1944
1923	Winslow, George Edgar	Hyde Park	April 17, 1944
1907	Wood, Benjamin Ezra	Canton	December 26, 1943
1928	Wright, Allen Henry	East Northfield	June 17, 1943
1895	†Wylie, Eugene Cushman	Dorchester	September 15, 1943
1915	†Young, Annie Roberts	Waltham	March 16, 1943
1924	Yudin, Hyman	Beverly	December 18, 1943

†Retired fellow.

Total number of deaths of active fellows	83
Total number of deaths of retired fellows	21
Total number of deaths of honorary fellows	1
Grand total	105

OFFICERS FOR 1944-1945

PRESIDENT: Elmer S. Bagnall, Groveland, 281 Main Street.
PRESIDENT-ELECT: Reginald Fitz, Brookline. Office, Boston, 319 Longwood Avenue.
VICE-PRESIDENT: Sumner H. Remick, Waltham, 735 Trapelo Road.
SECRETARY: Michael A. Tighe, Lowell. Office, Boston, 8 Fenway.
TREASURER: Eliot Hubbard, Jr., Cambridge, 29 Highland Street.
ASSISTANT TREASURER: Norman A. Welch, West Roxbury. Office, Boston, 520 Commonwealth Avenue.
ORATOR: Frank H. Lahey, Boston, 605 Commonwealth Avenue.

COMMITTEES ELECTED BY THE DISTRICTS

Executive Committee of the Council—Established 1941 (members *ex-officio* and one councilor and alternate elected by the councilors of each district medical society).

PRESIDENT: Elmer S. Bagnall, Groveland, 281 Main Street.
PRESIDENT-ELECT: Reginald Fitz, Brookline. Office, Boston, 319 Longwood Avenue.
VICE-PRESIDENT: Sumner H. Remick, Waltham, 735 Trapelo Road.
SECRETARY: Michael A. Tighe, Lowell. Office, Boston, 8 Fenway.
TREASURER: Eliot Hubbard, Jr., Cambridge, 29 Highland Street.

Term Expires 1945

ESSEX SOUTH: Loring Grimes, Swampscott, 84 Humphrey Street. (Alternate: Charles L. Curtis, Salem, 10 Federal Street.)
HAMPSHIRE: L. Beverly Pond, Easthampton, 115 Main Street. (Alternate: Joseph D. Collins, Northampton, 187 Main Street.)
MIDDLESEX SOUTH: Dwight O'Hara, Waltham. Office, Boston, 416 Huntington Avenue. (Alternate: Arthur M. Jackson, Everett, 512 Broadway.)
NORFOLK SOUTH: Henry A. Robinson, Hingham, 205 North Street. (Alternate: Nahum R. Pillsbury, South Braintree, Norfolk County Hospital.)
SUFFOLK: Donald Munro, Boston, 818 Harrison Avenue. (Alternate: Charles C. Lund, Boston, 319 Longwood Avenue.)
WORCESTER: Ralph S. Perkins, Worcester, 10 Hackfeld Road. (Alternate: Gordon Berry, Worcester, 36 Pleasant Street.)

Term Expires 1946

BARNSTABLE: William D. Kinney, Osterville.
BRISTOL NORTH: William H. Allen, Mansfield, 70 North Main Street. (Alternate: Ralph M. Chambers, Taunton State Hospital.)
BRISTOL SOUTH: Edwin D. Gardner, New Bedford, 11 Cottage Street. (Alternate: Richard B. Butler, F. River, 278 North Main Street.)
ESSEX NORTH: Frank W. Snow, Newburyport, 24 Essex Street. (Alternate: Rolf C. Norris, Methuen, 24 Broadway.)
MIDDLESEX EAST: Edward M. Halligan, Reading, 37 Sale Street. (Alternate: Richard Dutton, Wakefield, 1 Avon Street.)
PLYMOUTH: Peirce H. Leavitt, Brockton, 129 West Elm Street. (Alternate: Charles D. McCann, Brockton, 1 Cottage Street.)

Term Expires 1947

BERKSHIRE: Isaac S. F. Dodd, Pittsfield, 34 Fenn Street. (Alternate: Patrick J. Sullivan, Dalton, 471 Main Street.)
FRANKLIN: William J. Pelletier, Turners Falls, 113 Avenue. (Alternate: Merritt B. Low, Deerfield, 31 Federal Street.)
HAMPDEN: William A. R. Chapin, Springfield, 121 Chestnut Street. (Alternate: Edward P. Bagg, Holyoke, 207 Elm Street.)
MIDDLESEX NORTH: William F. Ryan, Lowell, 219 Central Street. (Alternate: William M. Collins, Lowell, 17 Central Street.)
NORFOLK: Charles J. Kickham, Brookline. Office, Boston, 524 Commonwealth Avenue. (Alternate: Henry M. Emmons, Boston, 354 Commonwealth Avenue.)
WORCESTER NORTH: C. Bertram Gay, Fitchburg, 62 Dana Street. (Alternate: Francis A. Reynolds, Athol, 4 Cottage Street.)

Committee on Public Relations—Established 1931 (one councilor elected yearly by each district medical society the president and president-elect of the Society are chairman and vice-chairman, respectively, and the vice president and secretary of the Society are members *ex-officio*).

BARNSTABLE: William D. Kinney, Osterville.
BERKSHIRE: Patrick J. Sullivan, Dalton, 471 Main Street.
BRISTOL NORTH: James H. Brewster, Attleboro, 178 South Main Street.
BRISTOL SOUTH: Harold E. Perry, New Bedford, 159 Cottage Street.
ESSEX NORTH: Harold R. Kurth, Lawrence, 57 Jackson Street.
ESSEX SOUTH: Loring Grimes, Swampscott, 84 Humphrey Street.

ANKLIN: William J. Pelletier, Turners Falls, 113 Avenue A.
 AMPDEN: Patrick E. Gear, Holyoke, 188 Chestnut Street.
 AMPSHIRE: Alfred J. Bonneville, Hatfield, 60 Main Street.
 MIDDLESEX EAST: J. Harper Blaisdell, Winchester. Office, Boston, 45 Bay State Road.
 MIDDLESEX NORTH: Daniel J. Ellison, Lowell, 8 Merrimack Street.
 MIDDLESEX SOUTH: John P. Nelligan, Cambridge, 2336 Massachusetts Avenue.
 ORFOLK: Norman A. Welch, West Roxbury. Office, Boston, 520 Commonwealth Avenue.
 ORFOLK SOUTH: Fred A. Bartlett, Wollaston, 308 Beale Street.
 YMOUTH: Charles D. McCann, Brockton, 12 Cottage Street.
 FFOLK: Albert A. Hornor, Boston, 319 Longwood Avenue. (Secretary.)
 WORCESTER: John Fallon, Worcester, 390 Main Street.
 WORCESTER NORTH: James V. McHugh, Leominster, 100 Main Street.

Committee on Legislation — Established 1942 (one councilor elected yearly by each district medical society).

ARNSTABLE: Julius G. Kelley, Pocasset, Barnstable County Sanatorium.
 ERKSHIRE: Clement F. Kernan, Pittsfield, 184 North Street.
 RISTOL NORTH: Ralph M. Chambers, Taunton, Taunton State Hospital.
 RISTOL SOUTH: Edwin D. Gardner, New Bedford, 150 Cottage Street.
 ESSEX NORTH: Edward H. Ganley, Methuen, 251 Broadway.
 ESSEX SOUTH: Charles A. Worthen, Lynn, 19 Park Street.
 FRANKLIN: Howard M. Kemp, Greenfield, 42 Franklin Street.
 HAMPDEN: William A. R. Chapin, Springfield, 121 Chestnut Street.
 HAMPSHIRE: Arthur N. Ball, Northampton, Northampton State Hospital.
 MIDDLESEX EAST: John M. Wilcox, Woburn, 6 Bennett Street.
 MIDDLESEX NORTH: Archibald R. Gardner, Lowell, 16 Shattuck Street.
 MIDDLESEX SOUTH: Brainard F. Conley, Malden, 51 Main Street (Chairman).
 NORFOLK: Humphrey L. McCarthy, West Roxbury. Office Boston, 479 Beacon Street.
 NORFOLK SOUTH: David L. Belding, Hingham. Office, Boston, 80 East Concord Street.
 PLYMOUTH: John J. McNamara, Brockton, 231 Main Street.
 SUFFOLK: William E. Browne, Boston, 587 Beacon Street.
 WORCESTER: Lester M. Felton, Worcester, 36 Pleasant Street.
 WORCESTER NORTH: Francis A. Reynolds, Athol, 43 Cottage Street.

Committee on Nominations — Established 1874 (one councilor and alternate elected yearly by each district medical society).

BARNSTABLE: William D. Kinney, Osterville. (Alternate: Paul M. Butterfield, Harwich.)
 BERKSHIRE: Patrick J. Sullivan, Dalton, 471 Main Street. (Alternate: Charles F. Fasce, Pittsfield, 311 North Street.)
 BRISTOL NORTH: William H. Allen, Mansfield, 70 North Main Street. (Alternate: Joseph L. Murphy, Taunton, 23 Cedar Street.)
 BRISTOL SOUTH: Edmond F. Cody, New Bedford, 105 South 6th Street. (Alternate: Richard B. Butler, Fall River, 278 North Main Street.)
 ESSEX NORTH: Guy L. Richardson, Haverhill, 94 Emerson Street. (Alternate: Rolf C. Norris, Methuen, 247 Broadway.)
 ESSEX SOUTH: Paul E. Tivnan, Salem, 70 Washington Street. (Alternate: Peer P. Johnson, Beverly, 1 Monument Square.)

FRANKLIN: Howard M. Kemp, Greenfield, 42 Franklin Street. (Alternate: William J. Pelletier, Turners Falls, 113 Avenue A.)
 HAMPDEN: Allen G. Rice, Springfield, 146 Chestnut Street. (Alternate: to be appointed.)
 HAMPSHIRE: L. Beverly Pond, Easthampton, 115 Main Street. (Alternate: Joseph D. Collins, Northampton, 187 Main Street.)
 MIDDLESEX EAST: Ralph R. Stratton, Melrose, 538 Lynn Fells Parkway. (Alternate: Edward M. Halligan, Reading, 37 Salem Street.)
 MIDDLESEX NORTH: Herbert M. Larrabee, Tewksbury. Office, Lowell, 9 Central Street. (Alternate: William M. Collins, Lowell, 174 Central Street.)
 MIDDLESEX SOUTH: Dwight O'Hara, Waltham. Office, Boston, 416 Huntington Avenue. (Alternate: Joseph C. Merriam, Framingham, 198 Union Avenue.)
 NORFOLK: David D. Scannell, Jamaica Plain. Office, Boston, 475 Commonwealth Avenue. (Alternate: Harry J. Inglis, Chestnut Hill. Office, Boston, 43 Bay State Road.)
 NORFOLK SOUTH: Daniel B. Reardon, Quincy, 1186 Hancock Street. (Alternate: James E. Knowlton, Wollaston, 579 Hancock Street.)
 PLYMOUTH: Walter H. Pulsifer, Whitman, 26 Park Avenue. (Alternate: Bradford H. Peirce, South Hanson, Plymouth County Hospital.)
 SUFFOLK: William B. Breed, Boston, 264 Beacon Street. (Alternate: Albert A. Hornor, Boston, 319 Longwood Avenue.)
 WORCESTER: Royal P. Watkins, Worcester, 332 Main Street. (Alternate: William F. Lynch, Worcester, 390 Main Street.)
 WORCESTER NORTH: Bartholomew P. Sweeney, Leominster, 5 Gardner Place. (Alternate: Francis A. Reynolds, Athol, 43 Cottage Street.)

STANDING COMMITTEES FOR 1944-1945

ELECTED BY THE COUNCIL, May 22, 1944

PUBLICATIONS — Established 1825.		<i>Date of Appointment</i>
Richard M. Smith	June 6, 1933 (appointed chairman May 21, 1941)	
James P. O'Hare	June 9, 1936	
Conrad Wesselhoeft	June 2, 1937	
William B. Breed	February 7, 1940	
Oliver Cope	May 21, 1941	
ARRANGEMENTS — Established 1849.		
Roy J. Heffernan	May 25, 1942 (appointed chairman May 22, 1944)	
Sidney C. Wiggin	June 24, 1942	
G. Guy Bailey	November 13, 1942	
Harold G. Giddings	May 22, 1944	
Robert L. Goodale	May 22, 1944	
ETHICS AND DISCIPLINE — Established 1871.		
Ralph R. Stratton	June 9, 1936 (appointed chairman May 21, 1941)	
William J. Brickley	February 3, 1937	
Allen G. Rice	June 1, 1938	
Fred R. Jouett	May 21, 1940	
Archibald R. Gardner	May 21, 1941	
MEDICAL EDUCATION — Established 1881.		
Robert T. Monroe	May 21, 1941 (appointed chairman February 4, 1942)	
George D. Henderson	June 1, 1938	
Chester S. Keefer	February 4, 1942	
Isaac R. Jankelson	May 25, 1942	
Arthur W. Allen	May 24, 1943	

MEMBERSHIP — Established 1897.

Harlan F. Newton	June 9, 1931 (appointed chairman May 25, 1942)
John E. Fish	June 17, 1930
Peirce H. Leavitt	June 1, 1938
Sumner H. Remick	May 24, 1943
Samuel N. Vose	March 15, 1944
William H. Allen, H. Quimby Gallupe, Albert E. Parkhurst	— representing the Supervising Censors.

PUBLIC HEALTH — Established 1912.

Roy J. Ward	May 22, 1944 (chairman)
Edward G. Huber	May 22, 1944
Ernest M. Morris	May 22, 1944
Dwight O'Hara	May 22, 1944
Conrad Wesselhoeft	July 27, 1944 (interim appointment)

MEDICAL DEFENSE — Established 1927.

Arthur W. Allen	June 7, 1927 (appointed chairman June 7, 1939)
Edwin D. Gardner	June 7, 1927
William R. Morrison	June 9, 1936 (sec. pro tem)
Horatio Rogers	June 7, 1939
Ira M. Dixon	August 17, 1942

SOCIETY HEADQUARTERS — Established 1942.

J. Harper Blaisdell	May 22, 1944 (chairman)
Charles G. Mixer	June 8, 1942
Michael A. Tighe	May 24, 1943
Frank R. Ober	May 22, 1944
Daniel B. Reardon	May 22, 1944

FINANCE — Established 1938.

Francis C. Hall	July 8, 1943 (chairman)
Ernest L. Hunt	June 2, 1938
Charles F. Wilinsky	June 2, 1938
Edward J. O'Brien, Jr.	June 2, 1938
Peer P. Johnson	October 4, 1939

INDUSTRIAL HEALTH — Established 1942.

Dwight O'Hara	May 25, 1942 (chairman)
Thomas L. Shipman	May 25, 1942 (appointed vice-chairman May 22, 1944)
Joseph C. Aub	May 25, 1942
Daniel L. Lynch	May 25, 1942
John R. Agnew	May 22, 1944
Louis R. Daniels	May 22, 1944
John G. Downing	May 22, 1944

ADVISORY COMMITTEE TO COMMITTEE ON INDUSTRIAL HEALTH — Established 1942.

Manfred Bowditch, Alton S. Pope, Irving R. Tabershaw.

SPECIAL COMMITTEES

COMMITTEE ON CANCER — Established 1917.

George A. Moore (Brockton), *chairman*; Franklin G. Balch, Sr., Ernest M. Daland, Channing C. Simmons, Thomas J. Anglem.

REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL.

William D. Kinney, George D. Henderson, Robert B. Osgood, Merrill E. Champion, Roy J. Ward.

COMMITTEE ON POSTGRADUATE INSTRUCTION — Established 1932.

Reginald Fitz, *chairman*; Leroy E. Parkins, *secretary*; Joseph W. O'Connor, Robert N. Nye, Charles J. Kickham.

COMMITTEE ON PHYSICAL THERAPY — Established 1935.

Arthur L. Watkins, *chairman*, Franklin P. Le Robert B. Osgood.

COMMITTEE TO CONSIDER EXPERT TESTIMONY — Established 1936.

Frank R. Ober, *chairman*; David Cheever, Francis McCarthy, Carl Bearse, William J. Brickley.

TWENTY-FIVE VOTING MEMBERS IN MASSACHUSETTS HEALTH SERVICE, INC. — Established 1939.

Benjamin H. Alton, Gerardo M. Balboni, William Breed, Laurence D. Chapin, Lucien R. Chas Hilbert F. Day, Augustus W. Dudley, John F. George K. Fenn, Joseph E. Flynn, Archibald Gardner, Henry W. Godfrey, John H. Lam Alexander A. Levi, Joseph C. Merriam, Du Munro, Albert E. Parkhurst, Helen S. Pitt Allen G. Rice, Arthur T. Ronan, Frank W. S George L. Steele, Ralph R. Stratton, John Talbot, Edward L. Young.

COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL COSTS INSURANCE — Established 1940.

James C. McCann, *chairman*; Peirce H. Leavitt, Jr. C. Merriam, J. Harper Blaisdell, Merrill C. Sos

COMMITTEE ON TAX-SUPPORTED MEDICAL CARE — Established 1940.

John J. Dumphy, *chairman*; Albert A. Hornor, W. J. Pelletier, Frederick S. Hopkins, Frank W. St

COMMITTEE TO MEET WITH THE MASSACHUSETTS HOSPITAL ASSOCIATION — Established 1940.

Walter G. Phippen, *chairman*; Frederic Hagler, E. D. Gardner, Albert E. Parkhurst, Edward Adams, John Fallon.

COMMITTEE ON MATERNAL WELFARE — Established 1944.

Louis E. Phaneuf, *chairman*; Richard M. Smith, *chairman*; Thomas Almy, Robert L. DeNorma Arthur F. G. Edgelow, Joseph W. O'Connor, mond S. Titus, Richard J. Williams, Warren Sisson, James M. Baty, Stewart H. Clifford, A M. Kimberly, Florence L. McKay, Robert Moulton, Daniel J. Ellison, Ralph E. Cole (in appointment), Benjamin deF. Lambert (in appointment).

COMMITTEE ON REHABILITATION — Established 1941.

William E. Browne, *chairman*; William M. Collins, J. J. Regan, Benjamin F. Andrews, Ralph M. C bers, Arthur L. Watkins, John Fallon.

COMMITTEE ON POSTPAYMENT MEDICAL CARE — Established 1942.

Daniel J. Ellison, *chairman*; Harold F. Rowley, Cf F. Fasce, James H. Brewster, Harold E. F Lucien R. Chaput, Loring Grimes, Howard Kemp, Patrick E. Gear, Alfred J. Bonneville, W L. McKenzie, Egon E. Kattwinkel, Norma Welch, Daniel B. Reardon (interim appointment), Michael F. Barrett, Francis T. Jantzen, James Brosnan, William G. LeBrecht.

MILITARY POSTGRADUATE COMMITTEE — Established 1941.

W. Richard Ohler, *chairman*; Leroy E. Parkins, *secretary*; Chester S. Keefer, Samuel H. Proger, F R. Ober, Gordon M. Morrison.

WAR PARTICIPATION COMMITTEE — Established 1943.

Guy L. Richardson, *chairman*; Ralph R. Stra Dwight O'Hara, Michael A. Tighe, Carl B Harold G. Giddings.

MEDICAL ADVISORY COMMITTEE TO REGIONAL OFFICE — Established 1943.

Joseph Garland, *chairman*; F. Gorham Brigham, Frank W. White, Loring Grimes (interim appointment).

STUAR LOAN FUND COMMITTEE — Established 1943.

George L. Schadt, *chairman*; Edward P. Bagg, C. Sidney Burwell, John Homans, Eliot Hubbard, Jr., Peirce H. Leavitt, Herbert L. Lombard, Hyman Morrison, Walter G. Phippen, William F. Ryan, David D. Scannell, Charles A. Sparrow, Ralph R. Stratton, Michael A. Tighe, Charles F. Wilinsky.

COMMITTEE TO LOOK INTO THE POSSIBILITY OF BETTER PUBLICITY FOR THE MASSACHUSETTS MEDICAL SOCIETY — Established 1943.

Albert A. Hornor, *chairman*; Michael A. Tighe, Robert N. Nye, Norman A. Welch, Walter H. Pulsifer.

COMMITTEE ON MEDICAL INFORMATION BUREAU — Established 1944.

Walter G. Phippen, *chairman*; Michael A. Tighe, Arthur W. Allen.

REPRESENTATIVE TO MENTAL HEALTH FOR DEFENSE ORGANIZATION

Abraham Myerson.

REPRESENTATIVE TO THE HOSPITAL COUNCIL OF BOSTON FOR THE YEAR 1944.

William E. Browne.

REPRESENTATIVE ON THE MASSACHUSETTS COMMITTEE FOR NURSES PROCUREMENT AND ASSIGNMENT SERVICE.

Dwight O'Hara.

REPRESENTATIVE ON THE LEGISLATIVE COMMITTEE OF THE MASSACHUSETTS CENTRAL HEALTH COUNCIL.

William E. Browne.

DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES, AMERICAN MEDICAL ASSOCIATION FOR 1944-1945

DELEGATES

ALTERNATES

June 1, 1943, to June 1, 1945

Allen G. Rice, Springfield
Richard H. Miller, Boston

Patrick J. Sullivan, Dalton
John Fallon, Worcester

June 1, 1944, to June 1, 1946

David D. Scannell, Jamaica Plain
Dwight O'Hara, Waltham
Charles E. Mongan, Somerville
Walter G. Phippen, Salem

Elmer S. Bagnall, Groveland
Ernest L. Hunt, Worcester
Charles J. Kickham, Brookline
John I. B. Vail, Hyannis

MASSACHUSETTS MEDICAL SERVICE

Officers and Directors

James C. McCann, M.D., president
Philip M. Morgan, vice-president
Edmund L. Twomey, treasurer
J. Harper Blaisdell, M.D.
Daniel J. Boyle
Thomas G. Brown
Thomas G. Dignan
J. H. Humphrey
Ernest A. Johnson
Harold B. Leland
Charles E. Mongan, M.D.
Frank R. Ober, M.D.
P. A. O'Connell
Roswell F. Phelps
Oliver G. Pratt
Samuel A. Robins, M.D.
R. F. Cahalane, executive director, 230 Congress Street, Boston

Members of the Corporation

William H. Allen, M.D.
Elmer S. Bagnall, M.D.
William A. R. Chapin, M.D.
Isaac S. F. Dodd, M.D.
Reginald Fitz, M.D.
Edwin D. Gardner, M.D.
C. Bertram Gay, M.D.
Loring Grimes, M.D.
Edward M. Halligan, M.D.
Eliot Hubbard, Jr., M.D.
Charles J. Kickham, M.D.
William D. Kinney, M.D.
Peirce H. Leavitt, M.D.
Donald Munro, M.D.
Dwight O'Hara, M.D.
William J. Pelletier, M.D.
Ralph S. Perkins, M.D.
L. Beverly Pond, M.D.
Sumner H. Remick, M.D.
Henry A. Robinson, M.D.
William F. Ryan, M.D.
Frank W. Snow, M.D.
Michael A. Tighe, M.D.

COUNCILORS FOR 1944-1945

(ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1944.)

BARNSTABLE

J. N. Kelly, Orleans, River Rd., V. P.
P. M. Butterfield, Harwich, A. M. N. C.
C. H. Keene, Chatham, Seaview St.
J. G. Kelley, Pocasset, Barnstable County Sanatorium, Sec.
W. D. Kinney, Osterville, E. C., M. N. C.

BERKSHIRE

F. R. Smith, Pittsfield, 18 Bank Row, V. P.
N. N. Copeland, Pittsfield, 131 North St., Sec.
I. S. F. Dodd, Pittsfield, 34 Fenn St., E. C.
C. F. Fasce, Pittsfield, 311 North St., A. M. N. C.
C. F. Kernan, Pittsfield, 184 North St.
C. T. Leslie, Pittsfield, 18 Bank Row.
J. F. McLaughlin, Adams, 25 Park St.
Solomon Schwager, Pittsfield, 246 North St.
P. J. Sullivan, Dalton, 471 Main St., A. E. C., M. N. C.

BRISTOL NORTH

J. L. Murphy, Taunton, 23 Cedar St., V. P., A. M. N. C.
W. H. Allen, Mansfield, 70 North Main St., E. C., M. N. C.
J. H. Brewster, Attleboro, 178 South Main St.
R. M. Chambers, Taunton, Taunton State Hospital, A. E. C.
W. J. Morse, Attleboro, 34 Sanford St., Sec.
W. M. Stobbs, Attleboro, 63 Bank St.

BRISTOL SOUTH

Russell Wood, New Bedford, 160 William St., V. P.
G. W. Blood, Fall River, 82 New Boston Rd.
R. B. Butler, Fall River, 278 North Main St., A. E. C., M. N. C.
E. F. Cody, New Bedford, 105 South Sixth St., M. N. C.
J. A. Fournier, Fall River, 11 Choate St.
E. D. Gardner, New Bedford, 150 Cottage St., E. C.
F. M. Howes, New Bedford, 135 Cottage St.
H. E. Perry, New Bedford, 159 Cottage St.
R. H. Smith, Edgartown, North Water St.
A. H. Sterns, New Bedford, 31 Seventh St., Sec.
I. N. Tilden, Mattapoisett, Barstow St.
C. C. Tripp, New Bedford, 416 County St.
P. E. Truesdale, Fall River, 151 Rock St.

ESSEX NORTH

J. T. Batal, Andover, Office Lawrence, 281 Haverhill St., V. P.
E. S. Bagnall, Groveland, 281 Main St., President.
R. V. Baketel, Methuen, 7 Hampshire St.
G. J. Connor, Haverhill, 81 Merrimack St.
Elizabeth Councilman, Newburyport, 83 High St.
H. A. Fenton, Lawrence, 36 Winthrop Ave.
E. H. Ganley, Methuen, 251 Broadway
H. R. Kurth, Lawrence, 57 Jackson St., Sec.
P. J. Look, Andover, 115 Main St.
R. J. Neil, Methuen, 255 Broadway.

R. C. Norris, Methuen, 247 Broadway, A. E. C., A. M. MIDDLESEX NORTH
N. C.

G. L. Richardson, Haverhill, 94 Emerson St., M. N. C.
F. W. Snow, Newburyport, 24 Essex St., E. C.
C. F. Warren, Amesbury, 1 School St.

ESSEX SOUTH

E. D. Reynolds, Danvers, 48 High St., V. P.
Bernard Appel, Lynn, 281 Ocean St.
H. A. Boyle, Middleton, Essex Sanatorium.
D. S. Clark, Salem, 2 Oliver St.
C. L. Curtis, Salem, 10 Federal St., A. E. C.
R. E. Foss, Peabody, 125 Main St.
Loring Grimes, Swampscott, 84 Humphrey St., E. C.
P. P. Johnson, Beverly, 1 Monument Sq., A. M. N. C.
H. M. Lowd, Swampscott, 90 Burrill St.
B. B. Mansfield, Ipswich, 4 Green St.
A. E. Parkhurst, Beverly, Monument Sq.
O. S. Pettingill, Middleton, Essex Sanatorium.
W. G. Phippen, Salem, 31 Chestnut St., Ex-Pres.
G. S. Rust, Gloucester, 48 Pleasant St.
H. D. Stebbins, Salem, 26 Chestnut St., Sec.
P. E. Tivnan, Salem, 70 Washington St., M. N. C.
J. W. Trask, East Lynn, 90 Ocean St.
C. F. Twomey, East Lynn, 80 Ocean St.
C. A. Worthen, Lynn, 19 Park St.

FRANKLIN

K. H. Rice, South Deerfield, 141 Main St., V. P.
H. L. Craft, Ashfield, Sec.
H. M. Kemp, Greenfield, 42 Franklin St., M. N. C.
M. B. Low, Deerfield, 31 Federal St., A. E. C.
W. J. Pelletier, Turners Falls, 113 Ave. A., E. C., A. M. N. C.

HAMPDEN

J. E. Dwyer, Springfield, 146 Chestnut St., V. P.
F. H. Allen, Holyoke, 16 Fairfield St.
E. P. Bagg, Holyoke, 207 Elm St., A. E. C.
J. M. Birnie, Springfield, 146 Chestnut St., Ex-Pres.
H. F. Byrnes, Springfield, 6 Chestnut St.
W. A. R. Chapin, Springfield, 121 Chestnut St., E. C.
J. L. Chereskin, Springfield, 333 Bridge St.
A. J. Douglas, Westfield, 93 Elm St.
E. C. Dubois, Springfield, 174 Buckingham St.
G. L. Gabler, Holyoke, 4 Bullard Ave.
P. E. Gear, Holyoke, 188 Chestnut St.
Frederic Hagler, Springfield, 20 Maple St.
G. D. Henderson, Holyoke, 176 Chestnut St.
F. S. Hopkins, Springfield, 146 Chestnut St.
Charles Jurist, Springfield, 70 Chestnut St.
M. W. Pearson, Ware, 19 Pleasant St.
A. G. Rice, Springfield, 146 Chestnut St., M. N. C.
G. L. Schadt, Springfield, 44 Chestnut St., Ex-Pres.
J. A. Seaman, Longmeadow, Office Springfield, 20 Maple St.
G. C. Steele, West Springfield, 39 Church St., Sec.
G. L. Steele, Springfield, 20 Maple St.

HAMPSHIRE

A. N. Ball, Northampton, State Hospital, V. P.
A. J. Bonneville, Hatfield, 60 Main St.
J. D. Collins, Northampton, 187 Main St., A. E. C., A. M. N. C.
W. M. Dobson, Northampton, Veterans Administration Facility.
L. B. Pond, Easthampton, 115 Main St., E. C., M. N. C.
Mary P. Snook, Chesterfield, Sec.

MIDDLESEX EAST

J. H. Kerrigan, Stoneham, 481 Main St. V. P.
J. H. Blaisdell, Winchester, Office Boston, 45 Bay State Rd., C.
R. M. Burgoyne, Winchester, 15 Washington St.
Richard Dutton, Wakefield, 33 Avon St., A. E. C.
E. M. Halligan, Reading, 37 Salem St., E. C., A. M. N. C.
R. W. Layton, Melrose, 8 Porter St., Sec.
M. J. Quinn, Winchester, 44 Church St.
R. R. Stratton, Melrose, 538 Lynn Fells Parkway, M. N. C., C.
J. M. Wilcox, Woburn, 6 Bennett St.

J. J. Cassidy, Lowell, 9 Central St., V. P.
H. R. Coburn, Lowell, 202 Merrimack St.
W. M. Collins, Lowell, 174 Central St., A. E. C., A. M. N. C.

D. J. Ellison, Lowell, 8 Merrimack St.
A. R. Gardner, Lowell, 16 Shattuck St.
H. M. Larrabee, Lowell, 9 Central St., M. N. C.
B. D. Leahey, Lowell, 9 Central St., Sec.
W. F. Ryan, Lowell, 219 Central St., E. C.
M. A. Tighe, Lowell, 9 Central St., Secretary.

MIDDLESEX SOUTH

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C. F. Atwood, Arlington, 821 Massachusetts Ave.
E. W. Barron, Malden, Office Boston, 20 Ash St.
W. B. Bartlett, Concord, 28 Monument St.
Harris Bass, Everett, 351 Broadway.
J. M. Baty, Belmont, Office Brookline, 1101 Beacon St.
J. D. Bennett, West Somerville, 72 College Ave.
E. H. Bigelow, Framingham, Hotel Kendall, Ex-Pres.
W. O. Blanchard, Newton, 465 Centre St.
G. F. H. Bowers, Newton Highlands, 156 Woodward St.
Madelaine R. Brown, Cambridge, Office Boston, 141 Beacon St.
R. W. Buck, Waban, Office Boston, 5 Bay State Rd.
E. J. Butler, Cambridge, 25 Garden St.
J. F. Casey, Allston, Office Boston, 475 Commonwealth Avenue.
C. W. Clark, Newtonville, 363 Walnut St.
B. F. Conley, Malden, 51 Main St.
J. A. Daley, Natick, 36 Pond St. (interim appointment)
H. F. Day, Cambridge, 34 Kirkland St.
C. L. Derick, Newton Highlands, Office Boston, 41 Beacon St.
J. G. Downing, Newton, Office Boston, 520 Commonwealth Ave.
R. A. Drake, West Medford, 298 High Street.
C. W. Finnerty, West Somerville, 5 Pearson Rd.
H. Q. Gallupe, Waltham, 751 Main St.
Stanton Garfield, Concord, 20 Sudbury St.
F. W. Gay, Malden, 20 Park St.
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J. L. Golden, Medford, 86 Forest St.
A. D. Guthrie, Medford, 408 Salem St.
Eliot Hubbard, Jr., Cambridge, 29 Highland St., Treasurer.
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E. E. Kattwinkel, West Newton, 65 Sterling St.
A. A. Levi, Newton, Office Boston, 481 Beacon St., Sec.
F. P. Lowry, Newton, 313 Washington St.
A. N. Makechnie, Cambridge, 14 Upland Rd.
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E. J. O'Brien, Jr., Newton, Office Boston, 270 Commonwealth Ave.
Dwight O'Hara, Waltham, Office Boston, 416 Huntington Ave., E. C., M. N. C., C.
Fabyan Packard, Belmont, Office Boston, Soldiers' Field
L. G. Paul, Newton Centre, Office Boston, 270 Commonwealth Ave.
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S. H. Remick, Waltham, 735 Trapelo Rd., Vice-President
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E. S. A. Robinson, Newton Centre, Office Jamaica Plain, 375 South St.
M. J. Schlesinger, Newton, Office Boston, 330 Brookline Ave.
E. W. Small, Belmont, 68 Leonard St.
H. P. Stevens, Cambridge, 1 Craigie St.
H. W. Thayer, Newtonville, 355 Walnut St.
K. J. Tillotson, Waverley, McLean Hospital (interim appointment).
A. B. Toppa, Watertown, 289 Mt. Auburn St.

J. E. Vance, Natick, Office Boston, 29 Bay State Rd.
 Fresenius Van Nüys, Weston, 338 Boston Post Rd.
 C. F. Walcott, Cambridge, 81 Sparks St.
 A. L. Watkins, Arlington, Office Boston, Massachusetts
 General Hospital.
 B. M. Wein, Newton, Office Boston, 471 Commonwealth
 Ave.
 B. S. Wood, Weston, Office Waltham, 751 Main St.
 Alfred Worcester, Waltham, 314 Bacon St., Ex-Pres.
 Horhannes Zovickian, Watertown, 528 Mt. Auburn St.

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 St., V. P.
 J. R. Barry, West Roxbury, 1857 Centre St.
 Carl Bearse, Boston, 483 Beacon St.
 Arthur Berk, Brookline, Office Boston, 270 Common-
 wealth Ave.
 M. I. Berman, Dorchester, 1071 A Blue Hill Ave.
 G. F. Blood, Roslindale, 20 Belgrade Ave.
 J. E. Burns, Wellesley Hills, Office Boston, 475 Common-
 wealth Ave.
 J. H. Carey, Dorchester, 103 Melville Ave.
 D. J. Collins, Norwood, 100 Day St.
 William Dameshek, Brookline, Office Boston, 371 Com-
 monwealth Ave.
 G. L. Doherty, West Roxbury, Office Boston, 466 Com-
 monwealth Ave.
 H. M. Emmons, Needham, Office Boston, 354 Common-
 wealth Ave., A. E. C.
 J. C. V. Fisher, West Roxbury, 1811 Centre St.
 Susannah Friedman, Roxbury, Office Boston, 485
 Commonwealth Ave.
 B. A. Godvin, Jamaica Plain, Office Boston, 483 Beacon
 St.
 D. C. Goldfarb, Brookline, Office Boston, 483 Beacon
 St.
 J. B. Hall, Roxbury, 60 Windsor St.
 H. B. Harris, East Milton, Office Dorchester, 487
 Columbia Rd.
 R. J. Heffernan, Jamaica Plain, Office Brookline, 1101
 Beacon St., C.
 H. J. Inglis, Chestnut Hill, Office Boston, 43 Bay State
 Rd., A. M. N. C.
 P. J. Jakmauh, Milton, Office South Boston, 509 Broad-
 way.
 I. R. Jankelson, Jamaica Plain, Office Boston, 483
 Beacon St.
 C. J. Kickham, Brookline, Office Boston, 524 Common-
 wealth Ave., E. C.
 C. J. E. Kickham, Jamaica Plain, Office Boston, 12 Bay
 State Rd., Sec.
 E. L. Kickham, Brookline, Office Boston, 270 Common-
 wealth Ave.
 H. M. Landesman, Roxbury, Office Boston, 429 Marl-
 borough St.
 Timothy Leary, Jamaica Plain, Office Boston, 784
 Massachusetts Ave.
 D. S. Luce, Canton, 553 Washington St.
 C. M. Lydon, Dorchester, 276 Bowdoin St.
 D. L. Lynch, Roslindale, Office Boston, 245 State St.
 F. P. McCarthy, Milton, Office Boston, 371 Common-
 wealth Ave.
 H. L. McCarthy, West Roxbury, Office Boston, 479
 Beacon St.
 R. T. Monroe, Brookline, Office Boston, 270 Common-
 wealth Ave., C.
 F. J. Moran, Dedham, 395 Washington St.
 Hyman Morrison, Roxbury, Office Boston, 483 Beacon
 St.
 D. J. Mullane, Jamaica Plain, 776 Centre St.
 Abraham Myerson, Brookline, Office Boston, 475 Com-
 monwealth Ave. (interim appointment).
 M. W. O'Connell, West Roxbury, Office Boston, Boston
 City Hospital.
 G. W. Papen, Brookline, Office Boston, 31 Milk St.
 H. C. Petterson, West Roxbury, Office Boston, 29 Bay
 State Rd.
 Frederick Reis, Jamaica Plain, Office Boston, 416 Hunt-
 ington Ave.
 S. A. Robins, Roxbury, Office Boston, 636 Beacon St.

D. D. Scannell, Jamaica Plain, Office Boston, 475 Com-
 monwealth Ave., M. N. C.
 J. A. Seth, Milton, Office Boston, 47 Bay State Rd.
 Kathlyne S. Snow, Jamaica Plain, Office Boston, 466
 Commonwealth Ave.
 J. W. Spellman, Chestnut Hill, Office Brookline, 1101
 Beacon St.
 M. H. Spellman, Jamaica Plain, Office Boston, 475
 Commonwealth Ave.
 J. P. Treanor, Jr., Jamaica Plain, Office Brookline, 1101
 Beacon St.
 W. J. Walton, Dorchester, 106 Bowdoin St.
 S. H. Weiner, Roxbury, Office Boston, 524 Common-
 wealth Ave.
 N. A. Welch, West Roxbury, Office Boston, 520 Common-
 wealth Ave., Assistant Treasurer.

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 F. A. Bartlett, Wollaston, 308 Beale St.
 D. L. Belding, Hingham, Office Boston, 80 East Concord
 St.
 Harry Braverman, Quincy, 43 School St.
 Frederick Hinchcliffe, Cohasset, 117 South Main St.
 E. K. Jenkins, South Braintree, Norfolk County Hos-
 pital, Sec.
 J. E. Knowlton, Quincy, 579 Hancock St., A. M. N. C.
 N. R. Pillsbury, South Braintree, Norfolk County
 Hospital, A. E. C.
 D. B. Reardon, Quincy, 1186 Hancock St., M. N. C.

PLYMOUTH

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 S. J. Beers, Plymouth, 118 Court St.
 C. H. King, Duxbury, Cedar St.
 C. D. McCann, Brockton, 12 Cottage St., A. E. C.
 R. C. McLeod, Brockton, Goddard Hospital, Sec.
 J. J. McNamara, Brockton, 231 Main St.
 G. A. Moore, Brockton, 167 Newbury St.
 B. H. Peirce, South Hanson, Plymouth County Hospital,
 A. M. N. C.
 E. L. Perry, Middleboro, 39 Oak St.
 W. H. Pulsifer, Whitman, 26 Park Ave., M. N. C.

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Donald Munro, Boston, 818 Harrison Ave., V. P., E. C.
 A. W. Allen, Boston, 266 Beacon St., C.
 J. W. Bartol, Boston, 1 Chestnut St., Ex-Pres.
 W. B. Breed, Boston, 264 Beacon St., M. N. C.
 W. J. Brickley, Boston, 524 Commonwealth Ave.
 W. E. Browne, Boston, 587 Beacon St.
 W. B. Castle, Boston, Boston City Hospital.
 David Cheever, Boston, 193 Marlborough St.
 Pasquale Costanza, East Boston, 238 Maverick St.
 N. W. Faxon, Boston, Massachusetts General Hospital.
 G. B. Fenwick, Chelsea, 38 Cary Ave.
 Jacob Fine, Boston, 330 Brookline Ave.
 Reginald Fitz, Boston, 319 Longwood Ave., President-
 Elect.
 Somers Fraser, Boston, 395 Commonwealth Ave.
 Maurice Fremont-Smith, Boston, 12 Hereford St.
 Channing Frothingham, Boston, Office Jamaica Plain,
 1155 Centre St., Ex-Pres.
 Joseph Garland, Boston, 266 Beacon St.
 R. L. Goodale, Boston, 330 Dartmouth St., Sec.
 F. C. Hall, Boston, 372 Marlborough St., C.
 John Homans, Boston, 311 Beacon St. (interim
 appointment).
 A. A. Hornor, Boston, 319 Longwood Ave., A. M. N. C.
 L. M. Hurxthal, Boston, 605 Commonwealth Ave.
 C. S. Keefer, Boston, 65 East Newton St.
 H. A. Kelly, Winthrop, 200 Pleasant St.
 R. I. Lee, Boston, 264 Beacon St., Ex-Pres.
 C. C. Lund, Boston, 319 Longwood Ave., A. E. C.
 W. J. Mixer, Boston, 319 Longwood Ave.
 H. L. Musgrave, Revere, 622 Beach St.
 H. F. Newton, Boston, 319 Longwood Ave., C.
 R. N. Nye, Boston, 8 Fenway.
 F. R. Ober, Boston, 234 Marlborough St., Ex-Pres.
 F. W. O'Brien, Boston, 465 Beacon St.
 J. P. O'Hare, Boston, 520 Commonwealth Ave.

L. E. Parkins, Boston, 12 Bay State Rd.
 L. E. Phaneuf, Boston, 270 Commonwealth Ave.
 Helen S. Pittman, Boston, 264 Beacon St.
 J. H. Pratt, Boston, 30 Bennet St.
 J. J. Regan, Boston, 520 Commonwealth Ave. (interim appointment).
 W. H. Robey, Boston, 202 Commonwealth Ave., Ex-Pres.
 H. F. Root, Boston, 81 Bay State Rd.
 R. M. Smith, Boston, 330 Dartmouth St., C.
 M. C. Sosman, Boston, 721 Huntington Ave.
 E. F. Timmins, South Boston, 527 Broadway.
 J. J. Todd, Boston, 479 Beacon St.
 S. N. Vose, Boston, 29 Bay State Rd.
 Conrad Wesselhoeft, Boston, 315 Marlborough St.
 C. F. Wilinsky, Boston, 330 Brookline Ave.

WORCESTER

B. H. Alton, Worcester, 27 Elm St., V. P.
 C. R. Abbott, Clinton, 60 Walnut St.
 B. F. Andrews, Worcester, 36 Pleasant St.
 A. W. Atwood, Worcester, 390 Main St.
 George Ballantyne, Worcester, 27 Elm St.
 Gordon Berry, Worcester, 36 Pleasant St., A. E. C.
 W. P. Bowers, Clinton, 264 Chestnut St., Ex-Pres.
 E. J. Crane, Holden, Armington Lane.
 J. J. Dumphy, Worcester, 390 Main St.
 John Fallon, Worcester, 390 Main St.
 L. M. Felton, Worcester, 36 Pleasant St.
 J. V. Gallagher, Milford, 224 Main St.
 E. R. Leib, Worcester, 36 Pleasant St.
 L. P. Leland, Worcester, 36 Pleasant St., Sec.
 W. F. Lynch, Worcester, 390 Main St., A. M. N. C.
 J. C. McCann, Worcester, 390 Main St.
 A. E. O'Connell, Worcester, 390 Main St.
 H. L. Paine, North Grafton, Grafton State Hospital
 R. S. Perkins, Worcester, 10 Hackfeld Rd., E. C.
 C. A. Sparrow, Worcester, 21 West St.
 O. H. Stansfield, Worcester, 36 Pleasant St.
 T. L. Story, Southbridge, 17 Maple St. (interim appointment).
 J. C. Sullivan, Webster, 18 Negus St.
 R. J. Ward, Worcester, 9 Bellevue St., C.
 R. P. Watkins, Worcester, 332 Main St., M. N. C.
 B. C. Wheeler, Worcester, 27 Elm St.
 S. B. Woodward, Worcester, 58 Pearl St., Ex-Pres.

WORCESTER NORTH

H. D. Bone, Gardner, 19 Pleasant St., V. P.
 E. A. Adams, Fitchburg, 44 Oliver St., Sec.
 C. B. Gay, Fitchburg, 62 Day St., E. C.
 G. P. Keaveny, Fitchburg, 62 Fox St.
 J. V. McHugh, Leominster, 100 Main St.
 F. A. Reynolds, Athol, 43 Cottage St., A. E. C., A. M. N. C.
 B. P. Sweeney, Leominster, 5 Gardner Place, M. N. C.

The initials E. C. indicate that he is a member of the Executive Committee of the E. C. that he is an alternate member of the Executive Committee on Nominations and A. M. N. C. that he is an alternate member of the Committee on Nominations, V. P. that a member is a counselor by virtue of his office as president of a district society and so vice-president of the general society, C. by virtue of his office as chairman of a standing committee, Sec. by virtue of his office as secretary of a district society and Ex-Pres. by virtue of being a past president

CENSORS FOR 1944-1945

BARNSTABLE

W. D. Kinney, Osterville, *supervisor*.
 E. F. Curry, Sagamore.
 C. E. Harris, Hyannis.
 J. I. B. Vail, Hyannis.
 D. H. Hiebert, Provincetown.

BERKSHIRE

C. T. Leslie, Pittsfield, *supervisor*.
 I. S. F. Dodd, Pittsfield
 M. M. Brown, North Adams.
 A. C. England, Pittsfield,
 W. T. Frawley, Pittsfield.

BRISTOL NORTH

W. H. Allen, Mansfield, *supervisor*.
 L. E. Butler, Taunton.
 A. J. Leddy, Taunton.

J. H. Brewster, Attleboro.
 W. M. Stobbs, Attleboro.

BRISTOL SOUTH

(Supervisor to be appointed.)
 E. A. McCarthy, Fall River
 F. M. Howes, New Bedford.
 W. F. MacKnight, Fall River.
 C. C. Persons, New Bedford.

ESSEX NORTH

R. V. Baketel, Methuen, *supervisor*.
 L. C. Peirce, Newburyport.
 E. M. Gale, Merrimac.
 F. A. O'Reilly, Lawrence.
 W. W. Ferrin, Haverhill.

ESSEX SOUTH

A. E. Parkhurst, Beverly, *supervisor*.
 J. G. Adams, Salem.
 W. C. Inman, Danvers.
 R. A. Harpin, Lynn.
 I. B. Hull, Gloucester.

FRANKLIN

W. J. Pelletier, Turners Falls, *supervisor*.
 A. H. Ellis, Greenfield.
 P. M. Freeman, Greenfield.
 J. E. Moran, Greenfield.
 F. W. Dean, Northfield.

HAMPDEN

Frederic Hagler, Springfield, *supervisor*.
 J. M. Gilchrist, Springfield.
 A. F. G. Edgelow, Springfield.
 John Pallo, Westfield.
 G. D. Henderson, Holyoke.

HAMPSHIRE

A. J. Bonneville, Hatfield, *supervisor*.
 M. E. Cooney, Northampton.
 T. F. Corriden, Northampton.
 J. E. Hayes, Northampton.
 C. H. Wheeler, Haydenville.

MIDDLESEX EAST

M. J. Quinn, Winchester, *supervisor*.
 J. H. Fay, Melrose.
 C. E. Montague, Wakefield.
 S. H. Moses, Winchester.
 C. R. Baisley, Reading.

MIDDLESEX NORTH

W. F. Ryan, Lowell, *supervisor*.
 F. R. Brady, Lowell.
 R. C. Stewart, Lowell.
 H. L. Leland, Lowell.
 J. D. Sweeney, Lowell.

MIDDLESEX SOUTH

H. Q. Gallupe, Waltham, *supervisor*.
 E. H. Robbins, Somerville.
 A. N. Makechnie, Cambridge.
 J. E. Vance, Natick.
 H. W. Thayer, Newtonville.

NORFOLK

Hyman Morrison, Roxbury, *supervisor*.
 C. J. Kickham, Brookline.
 C. E. Allard, Dorchester.
 Saul Berman, Chestnut Hill.
 Kathlyne S. Snow, Jamaica Plain.

NORFOLK SOUTH

C. S. Adams, Wollaston, *supervisor*.
 D. L. Belding, Hingham.
 W. L. Sargent, Quincy.
 C. J. Lynch, Quincy.
 R. R. Ryan, South Weymouth.

MIDDLESEX

E. L. Perry, Middleboro, *supervisor*.
J. H. Dunn, Rockland.
J. A. Pettey, Brockton.
D. W. Pope, Brockton.
W. T. Hanson, Bridgewater.

NORFOLK

J. H. Pratt, Boston, *supervisor*.
H. T. Hutchins, Boston.
A. J. A. Campbell, Boston.
W. E. Browne, Boston.
E. F. Timmins, South Boston.

WORCESTER

B. C. Wheeler, Worcester, *supervisor*.
B. H. Flower, Shrewsbury.
George Ballantyne, Worcester.
R. S. Newton, Westboro.
H. N. Kelley, Worcester.

WORCESTER NORTH

C. B. Gay, Fitchburg, *supervisor*.
F. J. Djeri, Fitchburg.
G. P. Keaveny, Fitchburg.
J. A. McLean, Ayer.
F. A. Reynolds, Athol.

VICE-PRESIDENTS OF THE MASSACHUSETTS MEDICAL SOCIETY (*Ex-Officio*) FOR 1944-1945

PRESIDENTS OF DISTRICT MEDICAL SOCIETIES

(Arranged according to seniority of fellowship
in the Massachusetts Medical Society)

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BARNSTABLE NORTH — James J. Cassidy, Lowell.
BARNSTABLE SOUTH — Harold G. Giddings, Newton Centre.
BARNSTABLE EAST — Joseph H. Kerrigan, Stoneham.
BARNSTABLE WEST — John E. Dwyer, Springfield.
HAMPSHIRE — Arthur N. Ball, Northampton.
MIDDLESEX NORTH — Joseph L. Murphy, Taunton.
MIDDLESEX SOUTH — Henry A. Robinson, Hingham.
PLYMOUTH — Peirce H. Leavitt, Brockton.
WORCESTER NORTH — Herman D. Bone, Gardner.
WORCESTER — Benjamin H. Alton, Worcester.
NORFOLK — Donald Munro, Boston.
MIDDLESEX SOUTH — Russell Wood, New Bedford.
BARNSTABLE — Kenneth H. Rice, South Deerfield.
BARNSTABLE NORTH — John T. Batal, Lawrence.
HAMPSHIRE — Floyd R. Smith, Pittsfield.
BARNSTABLE SOUTH — Edwin D. Reynolds, Danvers.
BARNSTABLE — Joseph N. Kelly, Orleans.

COMMISSIONERS OF TRIAL FOR 1944-1945

BARNSTABLE — F. O. Cass, Provincetown.
HAMPSHIRE — J. B. Thomes, Pittsfield.
MIDDLESEX NORTH — J. W. Cook, Mansfield.
MIDDLESEX SOUTH — A. C. Lewis, Fall River.
BARNSTABLE NORTH — F. W. Anthony, Haverhill.
BARNSTABLE SOUTH — O. C. Blair, Lynn.
BARNSTABLE — K. W. D. Jacobus, Turners Falls.
BARNSTABLE — F. K. Dutton, Springfield.

HAMPSHIRE — E. H. Copeland, Northampton.
MIDDLESEX EAST — W. H. Keleher, Woburn.
MIDDLESEX NORTH — J. F. Boyle, Lowell.
MIDDLESEX SOUTH — H. P. Stevens, Cambridge.
NORFOLK — W. J. Walton, Dorchester.
NORFOLK SOUTH — F. A. Bartlett, Wollaston.
PLYMOUTH — J. A. Carriuolo, Brockton.
SUFFOLK — J. R. Torbert, Boston.
WORCESTER — W. P. Bowers, Clinton.
WORCESTER NORTH — A. P. Lachance, Gardner.

OFFICERS OF THE SECTIONS FOR 1945

ELECTED BY THE SECTIONS

SECTION OF MEDICINE

Chairman, Albert A. Hornor, Boston; *vice-chairman*, Daniel J. Ellison, Lowell; *secretary*, Francis C. Hall, Boston.

SECTION OF SURGERY

Chairman, Charles F. Twomey, East Lynn; *secretary*, Alexander J. A. Campbell, Boston.
Executive Committee — Stanley J. G. Nowak, Belmont and Boston (1 year); Edward L. Young, Jr., Brookline and Boston (2 years); E. Parker Hayden, Brookline and Boston (2 years).

SECTION OF PEDIATRICS

Chairman, Floyd R. Smith, Pittsfield; *secretary*, Gerald N. Hoefel, Cambridge.
Executive Committee — *Chairman*, Philip H. Sylvester, Boston; James Marvin Baty, Belmont and Brookline; Leroy T. Stokes, Haverhill.

SECTION OF OBSTETRICS AND GYNECOLOGY

Chairman, Arthur F. G. Edgelow, Springfield; *vice-chairman*, William J. McDonald, Boston; *secretary*, George Van S. Smith, Brookline.

SECTION OF RADIOLOGY

Chairman, George Levene, Chestnut Hill and Boston; *secretary*, Edward B. D. Neuhauser, Cambridge and Boston.

SECTION OF PHYSIOTHERAPY

Chairman, Arthur L. Watkins, Arlington and Boston; *secretary*, Howard Moore, Newton and Boston.

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Chairman, Bernard Appel, Lynn; *secretary*, Fenner A. Chace, Fall River.

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES FOR 1944-1945

BARNSTABLE — *President*, Joseph N. Kelly, Orleans; *vice-president*, Harold F. Rowley, Harwich Port; *secretary*, Julius G. Kelley, Pocasset; *treasurer*, Frank Travers, Barnstable; *librarian*, Carroll H. Keene, Chatham; *executive and public-relations counselor*, William D. Kinney, Osterville; *legislative counselor*, Julius G. Kelley, Pocasset.

BERKSHIRE — *President*, Floyd R. Smith, Pittsfield; *vice-president*, Thomas H. Nelligan, Pittsfield; *secretary*, N. Newall Copeland, Pittsfield; *treasurer*, Daniel N. Beers, Pittsfield; *executive counselor*, Isaac S. F. Dodd, Pittsfield; *legislative counselor*, Clement F. Kernan, Pittsfield; *public-relations counselor*, Patrick J. Sullivan, Dalton.

BRISTOL NORTH — *President*, Joseph L. Murphy, Taunton; *vice-president*, William M. Stobbs, Attleboro; *secretary*, William J. Morse, Attleboro; *treasurer*, Joseph V. Chatigny, Taunton; *executive councilor*, William H. Allen, Mansfield; *legislative councilor*, Ralph M. Chambers, Taunton; *public-relations councilor*, James H. Brewster, Attleboro.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30311

PRESENTATION OF CASE

A thirty-nine-year-old housewife was admitted to the hospital for study.

The patient had been in apparent good health until two years before entry when she experienced intermittent attacks of epigastric pain, following one year of "beer drinking and smoking almost incessantly." The pain was centered in the pit of the stomach and radiated to the right scapula. During the attacks she was unable "to sit or lie still or get her breath." Leaning forward and pressing against the stomach with a pillow brought relief. She was seen by her physician, who attributed her condition to drinking and prescribed some pills and a liquid, which gave some relief. The attacks recurred on an average of once a month and lasted for a few days. About nine months before entry the attacks became more frequent and more severe. At that time she had an episode of jaundice with chills, fever and pain that subsided spontaneously. Following this she had a severe attack of epigastric pain that radiated to the back and along both costal margins. The pain occurred after eating and was accompanied by copious vomiting. This episode lasted for a week, although she was temporarily relieved by medication. Eight months before entry she was admitted to a hospital in another city, where a history of intolerance for fatty and fried foods and a story of constipation for a year were elicited.

Physical examination at that time showed tenderness without spasm in the epigastrium, and tenderness in the left upper quadrant. The blood was normal. A Graham test was positive, although no stones were visualized. A cholecystectomy was performed, and palpation of the common duct revealed no stones. The gastric area was firm and adherent. The pathological diagnosis was chronic cholecystitis. Postoperatively she continued to have abdominal pain. A fluoroscopic examination of the stomach three weeks postoperatively showed a 2-cm. projection on the anterior wall near the lesser curvature and 5 cm. posterior to the pylorus, over which no

peristaltic wave seemed to pass. The films made at the time did not show this finding. Re-examination three weeks later was also inconclusive. In some positions there appeared to be a large ulcer on the posterior wall at about the junction of the middle and lower thirds. The rugae of the entire stomach were coarse and irregular.

A second exploratory laparotomy was performed seven weeks after the first operation. The viscera above the omentum appeared to be densely plastered together, and a preliminary Witzel jejunostomy was performed. The patient was placed on a Sippy diet for five weeks, without improvement. She was finally discharged after six months of hospitalization but readmitted three days later because of recurrence of pain. The gastric contents two weeks after readmission consisted mostly of bile, with no free acid and 20 units of combined acid.

The patient remained in the hospital until two weeks before transfer to this hospital. During that period of hospitalization she had lost 65 pounds. She claimed that she had as much epigastric pain as before operation, but its character was different. It appeared primarily on deep inspiration and radiated bilaterally along both costal borders to the shoulder and arm on the left side. The pain apparently had no relation to meals or to bowel movements. The latter were scanty, light colored and never bloody or tarry. She vomited only rarely. For three days before entry she had been free of pain.

Physical examination showed a well-developed woman in no distress. The heart and lungs were normal. There were an old appendectomy scar in the right lower quadrant, a left rectus scar, and a small cruciate scar in the left flank, all of which were well healed. There was tenderness in the upper abdomen, most marked in the epigastrium, which felt diffusely more tense and resistant than the rest of the abdomen; no definite masses were palpable. Pelvic examination was essentially negative.

The blood pressure was 140 systolic, 95 diastolic. The temperature was 98° F., the pulse 80, and the respirations 20.

The white-cell count was 7300, with 75 per cent neutrophils. The red-cell count was 2,120,000, with 7 gm. of hemoglobin. The urine was negative except for the sediment, which contained innumerable red cells and 6 to 8 white cells per high-power field. A blood Hinton test was negative. The blood non-protein nitrogen was 22.5 mg. per 100 cc., and the protein 7.7 gm.; the chloride was 97 milliequiv. per liter. Gastric analysis revealed no free acid in the fasting sample and 39 units after histamine. A gastrointestinal series showed a normal esophagus. Along the lesser curvature and posterior wall of the body of the stomach and extending down nearly to the angulus was a 7-cm. area of rigidity, which produced a filling defect (Fig. 1). The edges of the latter were smooth. There was no definite shelf, and the mucosal pattern, although slightly irregular,

*On leave of absence.

appeared preserved over the greater portion of this area. No crater could be demonstrated, although one small irregularity was noted that could have been the edge of a fold or a small crater. The remainder of the stomach and the duodenum were not remark-

veloped severe anorexia and was unable to take food by mouth. She was given intravenous fluids. The following day the pain became severer, radiating to both shoulders, the precordial region and the neck. A Levine tube alleviated the vomiting, and the pain

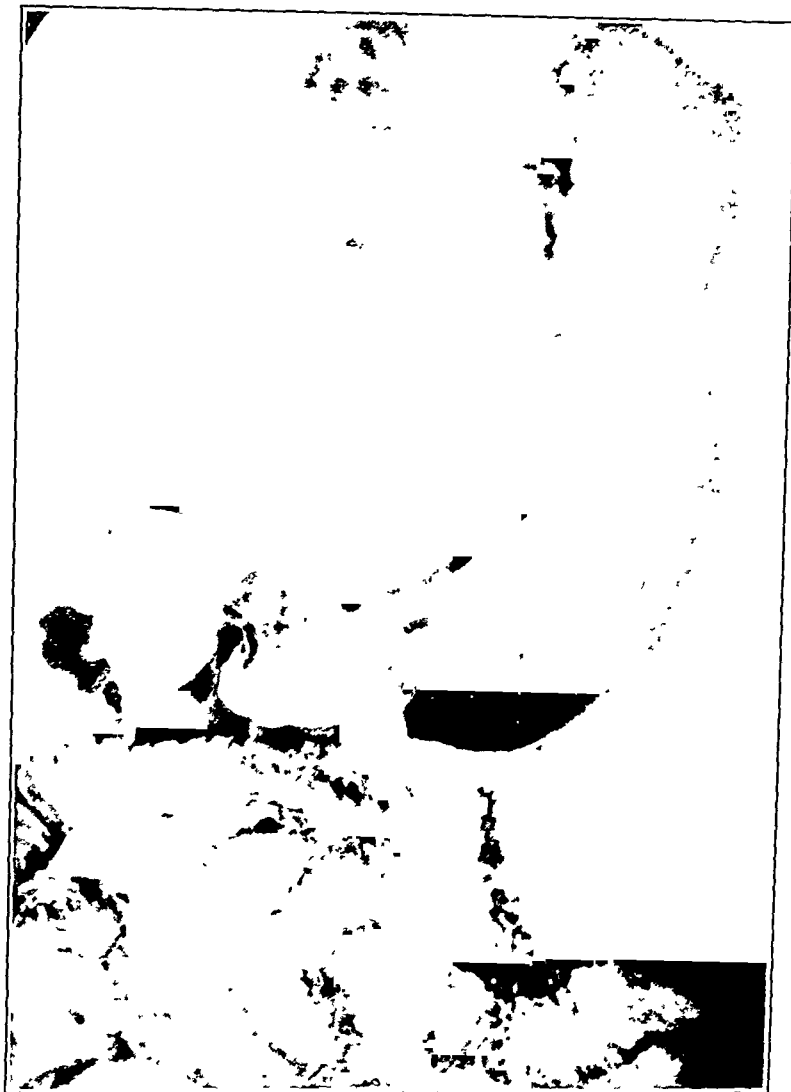


FIGURE 1. *Roentgenogram of the Stomach following a Barium Meal.*

able. Gastrosocopy on the second day revealed a normal antrum that appeared to be directed somewhat anteriorly. The body and lower portions of the fundus were well visualized, and the mucosa was everywhere intact. There were some adherent secretions on the posterior wall high in the body, and the mucosa in this region appeared fixed. There was no inflammation of the gastric mucosa.

The patient was placed on a six-meal bland diet and was given morphine for pain. For the first two days she did well. On the third day she had considerable retching and vomiting and abdominal pain. She de-

veloped severe anorexia and was unable to take food by mouth. She was then given daily intravenous fluids and several transfusions.

On the tenth hospital day an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: This thirty-nine-year-old patient was undoubtedly suffering from some form of gastric tumor. The original history quite obviously suggests gallstones, because she had pain in the epigastrium that radiated to the right scapula, and also associated with it she had one attack of jaundice.

the surgeon who saw her originally had a right suspect gall-bladder disease and cholelithiasis. She gave a story of having had copious vomiting. Copious vomiting in the presence of cholelithiasis is rather unusual and would have made me suspect that perhaps there was something in addition. I should also like to point out the fact that the Gram test was reported as positive, although no stones were visualized. It is our belief here — Dr. Robbins correct me if I am wrong — that just because the gall bladder does not show by cholecystogram does not mean disease of the gall bladder. It just means that the dye has not been absorbed in the biliary tract. I am never satisfied with the diagnosis of cholecystitis merely because of the absence of a gall-bladder shadow.

The operation bears out the fact that the gall bladder was not particularly abnormal. It was noted that that operation that she had some lesion in the region of the stomach, which apparently was not investigated too thoroughly. As a result of re-examination by x-ray she had a second exploratory laparotomy, and again the surgeon was unable to make up his mind what the trouble was in the stomach. They did a preliminary Witzel jejunostomy. I do not know why. We do a jejunostomy essentially for feeding purposes if we anticipate a major abdominal operation involving the stomach, so that we can get the patient into better condition. Possibly that is what was planned, but the patient was never in good condition for an operation.

DR. BENJAMIN CASTLEMAN: A portion of the operative note from the other hospital is as follows:

Under spinal anesthesia a left upper rectus incision was made and carried up to the sternum. The peritoneum, stomach, omentum and lesser curvature were all plastered down with edematous adhesive peritonitis. Below the omentum, however, there was no evidence of generalized peritonitis. The lesser peritoneum was opened by going through the gastrocolic ligament; this was found to be adhesive. There was no question of being able to do a gastrectomy. It was therefore decided that the best thing that could be done for the patient was to perform a Witzel jejunostomy for feeding purposes, thus by-passing the stomach.

DR. LINTON: When the patient was finally admitted here, the salient points about the laboratory examinations are that she had marked anemia and a hemoglobin of 7 gm. The urine contained many red cells, which we shall have to discount because we have no proof that it was a catheter specimen.

I should like to see the films of the gastrointestinal series that was done here.

DR. LAURENCE L. ROBBINS: This is the area along the lesser curvature in which the defect was found. It is best seen on the spot films. You will notice that the mucosa appears to be intact on all the spot films. There is only one thing that suggests the possibility of a minute ulceration, but it has more the appearance of a fold of the mucosa on end rather than a crater. I do not see anything that suggests the

shelflike margin of a carcinoma and certainly nothing that looks like a definite crater.

DR. LINTON: Examination of the stools bears that out, since they were negative for blood. Presumably there was no ulcer of the mucosa.

I am a little disturbed in making a diagnosis of tumor of the stomach in a patient who had had so much pain. I am unable to figure out why she had so much pain.

The first possibility is a gastric ulcer. That would explain the pain; but I do not see any evidence of it, and we have no other lead for that diagnosis. Apparently the pain was not affected by food, so I think that we can rule out ulcer on the history and also on the x-ray findings.

That leaves us with some kind of tumor of the stomach. The two that I am thinking of are a scirrhus type of carcinoma that had not ulcerated the gastric mucosa but was traveling in the submucosa and a leiomyoma or leiomyosarcoma. I believe that most leiomyosarcomas give a history of gastric hemorrhage, and this patient had no such history. The fact that she had lost a lot of weight and the fact that she had a marked secondary anemia make me think that she had a malignant lesion rather than a leiomyoma. For that reason I have to make the diagnosis of a scirrhus type of carcinoma of the stomach.

DR. FRANCIS D. MOORE: Were films of the chest taken? The patient had so much pleural pain on both sides around the costal margins that it would be interesting to see what the chest showed.

DR. ROBBINS: None were taken here. The chest was fluoroscoped during the gastrointestinal examination, and apparently nothing suspicious was observed.

DR. CASTLEMAN: None were taken at the other hospital.

CLINICAL DIAGNOSIS

Carcinoma of stomach.

DR. LINTON'S DIAGNOSIS

Carcinoma of stomach, scirrhus.

ANATOMICAL DIAGNOSES

Subdiaphragmatic and peritoneal abscess, left, old. Chronic adhesive peritonitis of upper abdomen, marked.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The operative note reads as follows:

The scar of the paramedian incision was excised. There were several areas of fat necrosis in the wound. A hard fixed mass involved the stomach and pancreas. This was adherent to the liver as well as to the retroperitoneal structures. The whole process felt like extensive malignant disease. There was no apparent fat necrosis inside the abdomen itself. The origin of the tumor could not be determined.

The patient died six days following operation. At autopsy, on opening the abdominal cavity, we found, especially on the left side, large numbers of dense, tough, fibrous adhesions. They involved the whole upper abdominal cavity, particularly the left subdiaphragmatic region. When the adhesions on the left side between the inferior surface of the stomach and the abdominal wall were separated, a large abscess was broken into; this measured about 10 by 4 by 3 cm. and apparently was the mass that was felt at the previous operation. A few small abscesses were also found. Further dissection showed only extensive adhesions. The mucosa and wall of the stomach were perfectly normal.

What the fundamental disease was at the onset of symptoms, I do not know; but I should guess that most of the pain that followed the first operation was due to the abscess and the extensive adhesions that were being formed.

DR. MOORE: Was this a colon-bacillus abscess?

DR. CASTLEMAN: The abscess was not cultured. The wall was thick and made up of granulation tissue. It must have been there for a long time.

DR. LINTON: The abstract gives only one temperature reading, which was 98°F. Did she have fever at any time?

DR. CASTLEMAN: The chart was normal except for one rise to 101°F.

DR. LINTON: Do you think that this was a pancreatitis with abscess formation?

DR. CASTLEMAN: We sectioned the pancreas and could not find any evidence of disease. We considered that diagnosis at the time of autopsy but found no evidence of fat necrosis except in the abdominal incision, which one finds without pancreatitis.

DR. LINTON: She still might have had a perforated ulcer.

DR. CASTLEMAN: We looked carefully for evidence of an old ulcer but could not find even a suspicious area.

It might be interesting to read the interpretation of the radiologist, which is as follows:

The findings are those of an area of rigidity along the lesser curvature of the body. It is possible that this represents intramural extramucosal involvement due to an inflammatory process as a result of a previously perforated ulcer. If one is to consider tumor, it would probably be one of the spindle-cell group. Suggest gastroscopy.

DR. ROBBINS: That was only because it had been reported to me that there had been an ulcer and I could not find it.

CASE 30312

PRESENTATION OF CASE

A forty-one-year-old Irish housewife was admitted to the hospital because of nausea and abdominal pain.

The patient had been in good health until about one year prior to admission, at which time she began

to experience nausea in the morning unassociated with meals and wearing off by noon. There was vomiting. She also noticed a tearing pain in the left upper quadrant of the abdomen on bending over. Eight months prior to entry she developed severe back pain, apparently in the region of the kidney coming on at night or during damp cold weather. She had had no hematuria or other urinary complaints. These attacks diminished as the weather became warmer. For about the same length of time she had noted a burning sensation over the left side of the face and extending downward to the breast and flank. During this period she had increasing fatigue. The nausea became progressively worse and was aggravated by food and exertion. During the three months prior to admission she developed a burning sensation in the hypogastrium associated with diminution in the burning over the face and chest, and a bearing-down sensation in the pelvis. On examination at another hospital she was told that her spleen was enlarged. She was referred to this hospital for study.

The family history except for renal disease in her mother, maternal aunt and maternal grandfather was noncontributory. The patient had worked in a rubber factory some years previously and had been exposed daily to benzol fumes over a period of eight years. For the three years prior to admission her menstrual periods had become irregular and scanty and she had been experiencing hot flashes, chill feelings and bouts of sweating, all of which had diminished in intensity.

Physical examination on admission revealed a well-developed and well-nourished woman in no discomfort. A few prominent veins were present on the chest. Several fixed nodes were felt in the right axilla. The heart and lungs were normal. The spleen was palpable five fingerbreadths below the costal margin, and was firm and nontender. The liver was not felt.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 99°F., the pulse 92, and the respirations 20.

Examination of the blood revealed a white-cell count of 3100, with 71 per cent neutrophils, 23 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils; there was some decrease in the platelets, and a definite shift of the neutrophils to the left, with numerous band forms. The red-cell count was 3,900,000, with 9 gm. of hemoglobin. The mean corpuscular volume was 97 millimicrons and the mean corpuscular hemoglobin 22 millimicrograms. The urine was repeatedly negative. The sedimentation rate was 42 mm. per hour, and 0.65 mm. per minute (corrected). The serum protein was 6.2 gm. per 100 cc., with an albumin-globulin ratio of 1.2. The blood cholesterol was 128 mg., the calcium 12.4 mg., and the phosphorus 3.9 mg. per 100 cc. The prothrombin time was normal. A bromsulfalein test revealed only 10 per cent re-

tion of the dye. A van den Bergh test and the urobilinogen were normal. A red-cell fragility test was normal. An agglutination test for brucella was negative. Tuberculin tests in dilutions up to 1:100 were negative. A blood Hinton reaction was negative. A gastric analysis revealed 47 units free acid thirty minutes after histamine.

An x-ray examination of the chest showed the right middle lobe to be slightly decreased in size, with areas of scarring and fibrosis; the remainder of the lung fields was clear. A plate of the abdomen revealed a markedly enlarged spleen, but the liver shadow was within normal limits. Roentgenographic examination revealed a normal esophagus. Examination of the femurs showed that the cortices of the lower portions of both bones were slightly thinner than normal, with a slight bulge about 10 cm. above their lower ends. The tibias, fibulas and humeruses were negative. A sternal bone-marrow biopsy revealed normal marrow.

On the twenty-sixth hospital day a splenectomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: I am going to tackle this problem by asking the question, Why was splenectomy performed?

The reasons for doing splenectomy, aside from a surgical condition such as splenic abscess or ruptured spleen, are hemolytic anemia, especially the familial hemolytic anemia, in which it is very successful, thrombopenic purpura, in which it is successful in 85 per cent of the cases, and perhaps thrombosis of the splenic vein, in which, in my experience, recurrence of hemorrhage, the reason for doing the splenectomy, is frequent. What else might one do it for? One may also take out a big spleen, such as the spleen found in Gaucher's disease, or occasionally in malaria, simply because it is so big. Of these possibilities everything has been ruled out except thrombosis of the splenic vein, and we have no evidence that such a condition was present. I shall come back to that in a moment.

I shall now take up the case from the clinical side. At the risk of being repetitious, I shall say in the first place that I think a blood smear in this case would be a fundamental thing to have seen, because the blood picture was peculiar and there is no mention here regarding the red cells—whether there was evidence of regeneration and polychromatophilia. In reading the history one gets the impression that something quite generalized was going on that had little to do with the weight of a large spleen. There were nausea and difficulty with food, neither of which has been explained. There was a tearing pain on bending over. Was that the pain of a large spleen, or pain from a lesion in the back? It seems to me that this was the pain of a lesion of the spine, with involvement of nerve roots. There was a burning sensation over the left side of the face, which also

involved the left side of the chest and flank—just where “the flank” is, I am never sure. How can one explain that? Was it on the basis of diffuse bone involvement, or was it a peripheral neuritis, or was it some sort of functional or emotional type of reaction? In addition, she had a bearing-down pain in the pelvis, which is hard to explain but may have been on the basis of some involvement of the nerve roots. The nausea is still unexplained.

Then we come to the question of exposure to benzol. I agree with Dr. Hunter that the safe amount of benzol to have in the air is zero. It is becoming more and more apparent that exposure to benzol can do anything to the blood picture. If there is exposure to large amounts of benzol, rather acute exposure, for weeks or months one finds the picture that we used to think was characteristic; that is, the process starts with granulocytopenia, goes on to thrombopenia and anemia and ends up with aplastic anemia or pancytopenia, an extremely serious clinical picture, which is sometimes relieved by transfusion. If there is exposure to minimal amounts of benzol over a long period of time one finds an entirely different picture: polycythemia, which is indistinguishable from true polycythemia, leukemia, which is indistinguishable from true leukemia, or finally a picture that has been referred to as “myeloid metaplasia” or extramedullary blood formation occurring in the spleen.

What about the picture we are presented with here? There was no granulocytopenia. In fact, the striking thing is that the leukopenia was a total leukopenia. This is not the picture that one sees with simply a congested spleen due to splenic-vein thrombosis or to portal cirrhosis, because when leukopenia results from a congested spleen it is almost always due to a reduction in the granulocytes. It is certainly not the picture that one sees with acute benzol poisoning. Furthermore, a bone-marrow biopsy was reported as negative. So, somewhat reluctantly, I am going to give up the idea that these findings were due to benzol poisoning.

Physical examination does not help us except for the fact that fixed nodes were felt in the right axilla. Apparently they did not make a great impression on the people taking care of this patient because nothing more is said about them.

DR. BENJAMIN CASTLEMAN: I might read what one observer said: “In the axilla there appear to be enlarged lymph nodes. If they are nodes, they are fixed.”

DR. RICHARDSON: That makes it a little different. I shall come back to the nodes in a minute.

Let me point out that the blood showed a macrocytic hypochromic anemia, which is striking and rather rare. When seen, it is usually in adults who have experienced blood loss for an unusually long period. There is no such story here, so that either the mean corpuscular volume was wrong or there were present in the blood smear large cells, probably

The patient died six days following operation. At autopsy, on opening the abdominal cavity, we found, especially on the left side, large numbers of dense, tough, fibrous adhesions. They involved the whole upper abdominal cavity, particularly the left subdiaphragmatic region. When the adhesions on the left side between the inferior surface of the stomach and the abdominal wall were separated, a large abscess was broken into; this measured about 10 by 4 by 3 cm. and apparently was the mass that was felt at the previous operation. A few small abscesses were also found. Further dissection showed only extensive adhesions. The mucosa and wall of the stomach were perfectly normal.

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DR. MEANS: I should like to take Dr. Richardson on one point. I do not believe that lack of evidence of esophageal varices rules out splenic-vein occlusion. I had a famous case with numerous varices in the stomach that neither the radiologist or the endoscopist could find, but the surgeon found them all right.

CLINICAL DIAGNOSIS

Splenomegaly.

DR. RICHARDSON'S DIAGNOSIS

Malignant lymphoma of spleen.

ANATOMICAL DIAGNOSIS

Sarcoid of spleen.

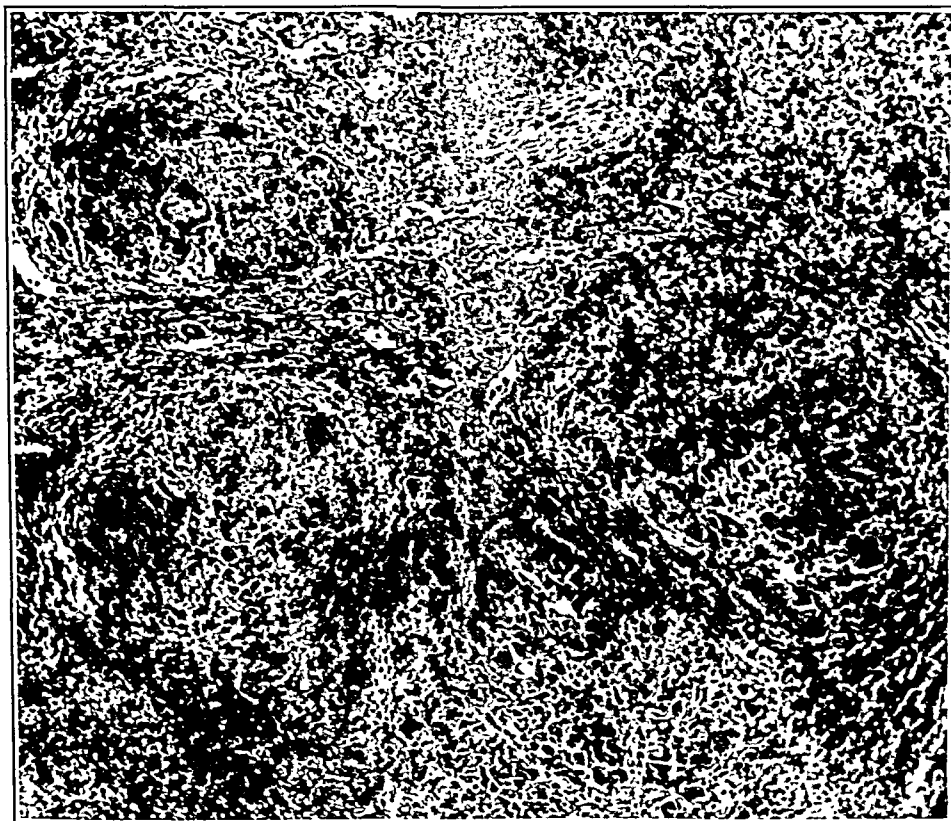


FIGURE 1. Photomicrograph of Section of Spleen.

DR. RICHARDSON: The patient we are discussing today did not bleed.

DR. MEANS: I meant merely that perhaps you are taking a risk in ruling out splenic-vein occlusion just because no varices were demonstrated.

DR. CASTLEMAN: Dr. William Dameshek was called in to see this patient. His note is as follows:

This patient has a very large, hard spleen, associated with leukopenia and probably thrombopenia. There is no evidence of hemolytic anemia, cirrhosis of the liver or lymphatic leukemia. Nor does the blood or bone-marrow picture show any evidence of myelogenous leukemia or myeloid metaplasia. The hypochromic anemia may be coincidental and might respond to iron. Gaucher's disease appears to have been ruled out. This leaves us with either a chronic infectious splenomegaly (? type), a Boeck's sarcoid or a primary neoplasm of the spleen. I think that the spleen is bulky enough and causing sufficient symptoms to be removed.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The spleen was about three times its normal size and was removed. Scattered throughout the parenchyma were round, ill-defined nodules 1.0 to 1.5 cm. in diameter, many of which produced a vague nodularity on the surface. Microscopically these proved to be lesions characteristic of sarcoid (Fig. 1).

The patient has been followed in the Out Patient Department for two years and is feeling well.

DR. RICHARDSON: What about the nodes?

DR. CASTLEMAN: They probably would show sarcoid. None were ever removed.

A chest plate taken a month or so ago shows no change.

immature polychromatophilic cells, that would have raised the mean corpuscular volume. The sedimentation rate (0.65 mm.) was definitely elevated. The calcium (12.4 mg.) was high, and the phosphorus (3.9 mg.) was on the high side of normal. Why was the calcium high? My thought is that the calcium was high because there was a destructive bone lesion. The bone was being destroyed, and calcium was being excreted. The phosphatase level might have been interesting but not too helpful. There was plenty of free hydrochloric acid. The rest of the laboratory tests were negative. I have reluctantly ruled out benzol poisoning. Were there any varices?

DR. LAURENCE L. ROBBINS: No.

DR. RICHARDSON: I rule out thrombosis of the splenic vein on the basis of the clinical picture, the lack of esophageal varices and the lack of a history of bleeding. There is no evidence of cirrhosis of the liver unless the presence of a normal-sized liver and an enlarged spleen is suggestive.

Is there any evidence of bone tumor in these x-ray films?

DR. ROBBINS: Except for thinning of the cortex in the lower portions of the femurs, the bones are not abnormal.

DR. RICHARDSON: There was some talk about a bulge.

DR. ROBBINS: It is not particularly abnormal.

DR. RICHARDSON: What about the middle lobe of the right lung?

DR. ROBBINS: I should think that that was probably an old process, with perhaps some bronchiectasis.

DR. RICHARDSON: How about carcinoma?

DR. ROBBINS: I see no sign of a mass or anything that suggests complete collapse; it is only partial atelectasis.

DR. RICHARDSON: What I am coming down to as a diagnosis is a diffuse malignant process involving the bone marrow. In such cases one usually gets a leukocytosis instead of a leukopenia, but I have seen several cases in which there was this type of leukopenia. I would feel better about it if there were definite evidence of red-cell regeneration in the blood smear.

What kind of tumor was it? Could it have been a myeloma? The patient was young. The total protein was normal, although the globulin was perhaps slightly elevated — and the albumin was a little low. There is no other evidence of myeloma.

Lymphoma may give this picture; I have seen an identical case. That again brings up the question of the axillary lymph nodes. If this patient had enlarged nodes, I submit that an axillary biopsy should have been done before splenectomy.

DR. CASTLEMAN: Another observer said; "There is one large lymph node in the left axilla."

DR. RICHARDSON: If there were enlarged nodes in either axilla I should have taken them out before

doing a splenectomy. We cannot, however, say that question now.

What other tumors should be considered? Nephroma ought to be, but there is no real evidence for it. Carcinoma in the lung? There are no symptoms suggesting it. Carcinoma elsewhere, perhaps of the stomach or pancreas? It would seem one should consider carcinoma of the stomach. I shall assume that that was ruled out, although it is not mentioned. Was a gastrointestinal one done?

DR. CASTLEMAN: There is no record of it.

DR. RICHARDSON: Of all the possibilities I mentioned it seems to me that lymphoma is likely but I should not be surprised if it were carcinoma. Again, I say that it is with reluctance that I rule up the possibility that benzol played a part, but do so definitely.

DR. J. H. MEANS: Did you mention any conditions for which one would not do splenectomy?

DR. RICHARDSON: The reasons that I mention for doing a splenectomy are hemolytic and thrombopenic purpura, splenic-vein thrombosis possibly a large spleen that is mechanically difficult to carry around, usually a Gaucher's spleen.

DR. MEANS: I simply wanted to be sure that I had heard all your reasons because I came to grief standing on the same spot that you are standing on more than twenty-four hours ago in one of these exercises put on for the third-year class. Most of the students made the correct diagnosis, but I did not. On the features in that case was a big spleen. I do suppose that the same diagnosis holds in this case but it is an interesting point to bring up in differential diagnosis of any large spleen.

DR. RICHARDSON: I also mentioned malaria.

DR. MEANS: It was not malaria.

DR. CASTLEMAN: Why not tell him what it was?

DR. MEANS: Sarcoid.

DR. RICHARDSON: I never thought of it.

DR. MEANS: Neither did I — yesterday.

DR. RICHARDSON: I do not believe that this patient had sarcoid.

DR. MEANS: Are those shadows around the lung roots normal?

DR. ROBBINS: From the film alone I think they are vascular shadows. Of course one would have to see them fluoroscopically. If they are vascular they are within the limits of normal; if they are lymph nodes, they are prominent.

DR. RICHARDSON: I believe that this was the form of malignant tumor involving the bone marrow and that the likeliest guess is lymphoma.

DR. MEANS: Why did they take the spleen out?

DR. RICHARDSON: Why did they? I think it was a great mistake to have taken it out.

DR. MEANS: Was the pathologist consulted about this? Was a frozen section done?

DR. CASTLEMAN: No.

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LYPHARMACY AND ANESTHESIA

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Many surgeons regularly use nurse anesthetists in their hospital practice, much to the chagrin of the anesthesiologists. Nurses, of course, are not always perfect anesthetists, but when well trained they do excellent work and, in general, heavy premedication is avoided, since the surgeon gives the orders.

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MASSACHUSETTS MEDICAL SOCIETY

WAR PARTICIPATION COMMITTEE

The accompanying certificate form (Fig. 1) has been adopted by the War Manpower Commission as the standard certificate for physicians to use when recommending change of employment for patients whose condition is or may be aggravated by continuance in their present jobs. The War Participation Committee has assisted in making this form as far as possible in order to save physicians' time and to give necessary information to the War Manpower Commission. The War Manpower Commission is of the opinion that physicians have been too easily prevailed on to issue certificates for change of employment. It is urged that physicians in giving these certificates exercise considerable care and discretion to make sure continuance in the present job is harmful to the patient.

The War Participation Committee has agreed to review the doctors' certificates, much in the same way that Dr.

MISCELLANY

ALVARENGA PRIZE

The College of Physicians of Philadelphia awarded the Alvarenga Prize on July 14, 1944, to Dr. Gervase J. Connor, of the Department of Surgery, Yale University School of Medicine, for an outstanding study entitled "Anterior Cerebellar Function: An analytical study in functional localization in the cerebellum in dog and monkey." This will be published in the December, 1944, issue of the *Transactions and Studies of the College of Physicians*.

The Alvarenga Prize was established by the will of Pedro Francisco da Costa Alvarenga, of Lisbon, Portugal, an associate fellow of the College of Physicians. "to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883, to the author of the best memorial upon any branch of medicine which may be deemed worthy of the prize." The College usually makes this award for outstanding published work and invites the

WORKER	Last Name	First	Middle	UNITED STATES EMPLOYMENT SERVICE of the WAR MANPOWER COMMISSION MEDICAL CERTIFICATE
	Address		Social Security Account No.	

1. How long have you been treating the worker named above? _____

2. Diagnosis? _____

3. Would continuance of his present job be injurious to the worker? ☐ Yes ☐ No

(a) If "yes," why? _____

4. What sort of work will his condition permit? _____

Form _____ Date _____ Signature _____ (Attending Physician)

This certificate approved by the War Participation Committee of the Massachusetts Medical Society. It is subject to review by that committee.

FIGURE 1.

Ireland's committee reviews physicians' applications for rationations from the various ration boards.

In summary, the War Participation Committee has agreed to assist the War Manpower Commission and to co-operate with it fully. The War Manpower Commission understands that our committee is interested in seeing that physicians are fairly and courteously treated by the district offices of the commission. In other words, we stand ready to try to adjust any complaints physicians have against the War Manpower Commission or its branches, as well as to review the certificates sent to the Commission.

GUY L. RICHARDSON, *Chairman*

DEATH

SPARKS — Ernest E. Sparks, M.D., of Cochrane, died July 21. He was in his seventy-second year.

Dr. Sparks received his degree from the University of Vermont College of Medicine in 1902. He established the Cochrane civilian-defense medical center. He was a member of the American Medical Association.

His widow survives.

recipient to deliver an Alvarenga Lecture before the College. The College occasionally, as in this instance, awards the prize for an exceptionally important manuscript submitted in competition.

CORRESPONDENCE

INDUSTRIAL MEDICAL CERTIFICATION

To the Editor: Not the least of the time-consuming chores given to the physician in modern society is that of certifying to this or that concerning his patients. Because of the physician's role among his fellowmen, he emerged early in our social development as the logical one to certify birth, to certify insanity and to certify the occurrence of contagious disease. With increased emphasis on public-health measures the physician has the task of examining food handlers and candidates for marriage for the purpose of certifying that these are ostensibly free of certain specific infections. The physician is deemed to be the logical citizen, in a democratic way of life, to perform these necessary functions.

With the rapid growth of the insurance principle during recent years, there has been an increase in the need for medical

OBITUARY

SIDNEY CHASE GRAVES

1901-1944

Lieutenant Commander Sidney Chase Graves, Medical Corps, U.S.N.R., died on May 14, 1944, in the Pacific area. No details concerning this tragedy are yet known except that he had been well but a few days before and that death did not occur in action. Until his departure earlier this year for an assignment overseas, he had been for eighteen months on duty at the United States Naval Hospital, Chelsea, Massachusetts.

Dr. Graves was born on July 21, 1901, at London, England, the first child of Alice Myrick (Chase) Graves and the late Dr. William Phillips Graves. Thereafter his life centered about Boston and Nantucket. He went to Noble and Greenough School, Boston, thence to St. Paul's School, Concord, New Hampshire, and prepared for college at Milton Academy, Milton, Massachusetts.

From Harvard College he entered the Harvard Medical School, receiving his degree in 1929. He acquired his clinical training first at the Massachusetts General Hospital and then at the Free Hospital for Women. He became a member of the staff of the latter in 1932, and was appointed assistant in gynecology at the Harvard Medical School in 1933. He carried on his private practice in Boston. He was a member of the American Medical Association, the Massachusetts Medical Society, the Boston Medical Library, the New England Obstetrical and Gynecological Society and the Obstetrical Society of Boston, a fellow of the American College of Surgeons and a diplomate of the American Board of Obstetrics and Gynecology.

In 1934 he married Alice Driver Brown of Philadelphia and is survived by her, their three children, his mother, a brother and a sister.

From his early school days his even disposition, cheerfulness and good comradeship made him the center of an admiring group of friends. As he progressed through school and college and



SIDNEY CHASE GRAVES

maturity, his characteristics came more manifest, so that he was known and liked by an ever increasing number of both with and without medical profession. He excelled in many sports and developed considerable skill in sketching, his habitual "doodling" consisted of drawings of animals, faces and amusing caricatures.

In professional work Dr. Graves showed great earnestness and one might say super-consciousness for the welfare of his patients, private and public. Their devotion was his reward. The good results of his reliable surgery are constantly evident in the follow-up

of his patents. For example, patients with tumors of the breast had been his special assignment for ten years at the Free Hospital for Women and the survival in cancer of the breast are now unusually high.

The happiness of his family life was obvious to all who entered his home and was affirmed in a tribute recently written by his wife. He left their "whole world." Those who knew him will remember him for his outstanding integrity, kindness, humor, sociability and sportsmanship. He leaves his many associates with a feeling that he was robbed of many useful, happy years and that a true friend who can never be replaced has been taken from them.

J. L. N. and G. V.

rapidly rising with the increased expectancy of life that resulted from advances in both curative and preventive medicine. It is stated in the foreword that it will not be before one third of the population of the United States is over fifty years of age, and it has been estimated that in forty years there will be twice as many people living more than sixty-five years than there are now. It is in the realm of possibility that the activities of pediatricians will become less whereas those of geriatricians will become more, although this is not an immediate probability. Marriage rates are raising the birth rates in many communities. With the constant reduction in infectious diseases, the number of persons living into the later decades has greatly increased and therefore there will be relatively larger numbers of cases of circulatory diseases with varied manifestations.

The editor discusses geriatrics ably and at some length, makes clear the fact that there is a wide difference between the aged and the aging. This is a point that some physicians and many of the laity overlook. An aged individual is one who has lived a considerable number of years and has therefore become, in common parlance, an old person. But an old person may have fewer signs of aging than one many years younger. Aging begins in the early years, and consequently the physician should have the objective and subjective signs of aging constantly in mind. That is one of the greatest pleas for the routine, regularly spaced, physical examination. To treat only those ill with a definite disease is after all, rather poor medicine.

The reviewer has read several books on geriatric medicine, although all are more or less treatises on general medicine. The present volume adheres more closely to the subject of aging than do any of the others. The editor has selected fifty-four authorities who have written with clarity on many important topics concerning the aging and the aged. From excellent discussions of circulatory, lung, bone, genitourinary, blood and metabolic diseases, there is much sound advice to assist the general practitioner in adjusting the aging to the changing conditions of their

Handbook of Medical Library Practice, including Annual Bibliographical Guides to the Literature and History of Medical and Allied Sciences. Based on a preliminary manuscript by M. Irene Jones and compiled by a committee of the Medical Library Association. Edited by Janet Doe. cloth, 610 pp. Chicago: American Library Association, 1934. \$5.00.

This pioneer work is a distinct contribution to the literature of medical librarianship. In the preface the editor states that the objective of the book is to discuss "library procedures, methods and subjects commonly used and found in medical libraries but different from those found in general libraries." These objectives are met, and the book is a manual of procedure, as well as a reservoir of useful data, for medical librarians. Its faults, mostly of omission and inadequate treatment of subjects, do not detract from the value of the book to the physician. They are technical in character and only affect the professional library worker.

The work is divided into eight chapters, each written by a member of the Medical Library Association. The first chapter is a general one and has to do with the medical library, its development, its distribution and its administration. Appended to this chapter are items of importance: first a list of all medical libraries, situated anywhere in the world, having 100,000 or more volumes, and the second a description of medical libraries located outside North America. The other chapters are more technical and discuss subjects as periodical and book selection, cataloguing, subject headings, classification, pamphlets, pictures and microfilms. The final chapters in the manual deal with rare books and the history of medicine, as well as reference work, including an annotated list of reference books. The essay on rare books and the history of medicine might well have been published separately, since it is more comprehensive than what the librarian of the average medical library needs. The shorter presentation of the subject, more dogmatic in character and featuring certain primary objectives, would have served the purpose better than the extended treatment indulged in by the author. The same can be said about the chapter on reference work. Much of the material in this

section, however, is of particular interest to medical collectors, historians and bibliographers.

The outstanding weakness of the book is the failure of the various authors to discuss the fundamental values of the various procedures and methods treated. Nowhere can be found any reference to the relative importance of the various topics. The student of medical librarianship and the inexperienced library worker in the field of medicine is left adrift, since little attempt is made to suggest the best procedures to be followed in her daily work. Some subjects are presented, moreover, without indication why they are included.

The editing is well done, and the level of writing is uniform for a collected work, although there are places where the English could have been improved.

The Principles and Practice of Industrial Medicine. Edited by Fred J. Wampler, M.D. 8°, cloth, 579 pp., with 42 illustrations and 36 tables. Baltimore: The Williams and Wilkins Company, 1945. \$6.00.

This is a selected group of thirty-three dissertations, each of which deals with a specialized problem in industrial medicine. It is not an elementary textbook.

Occasionally one of the contributors takes the bit in his teeth and runs away with his subject matter in a way that may well overwhelm the casual seeker after simple advice. It is possible to spread confusion rather than enlightenment by means of studies that are too erudite and elaborate. As a minor illustration, Dr. Foulger, of the Haskell Laboratory of Industrial Toxicology, finds it necessary to interpret blood-pressure readings on chemical workers with the aid of the formula,

$$\ln S = -0.00339 (x^2 + y^2),$$

where $\ln S$ is the logarithm of S (the score) to the base of 10, x the deviation of the diastolic blood pressure from an established mean of 79 mm., and y that of the pulse pressure from an established mean of 44 mm. This formula may be valid, and the conclusions reached in his study are interesting and probably significant, but a simpler presentation and interpretation would be more generally valuable in a textbook.

Topics covered include a variety of intoxications, the effects of temperature and humidity, the eyes, the back, compensation, women in industry, fatigue, the physical examination, the lay-out of medical departments and so forth. It is sadly ironic that the author of the excellent chapter on the cause and prevention of accidents should have been accidentally killed before his contribution appeared in print.

This book is recommended for reference reading.

Plastic Surgery of the Breast and Abdominal Wall. By Max Thorek, M.D., LL.D. With an introduction by Rudolf Nissen, M.D., and a foreword by J. Eastman Sheehan, M.D. 4°, cloth, 446 pp., with 458 illustrations. Springfield, Illinois: Charles C Thomas, 1942. \$6.00.

The main subject of this book is the treatment of the hypertrophied breast. The author has made a sincere effort to describe the various operative procedures advocated by the many surgeons who have taken a special interest in this field of surgery. He analyzes quite extensively the different operative procedures that seem best suited to each particular problem. There is included a short chapter on reconstructive surgery of the abdominal wall, and also chapters on the anatomy, physiology and pathology of the hypertrophied breast.

The book is profusely illustrated with good diagrams and photographic illustrations, and it is one of the most complete monographs on the subject that has come to the reviewer's attention.

Convulsive Seizures: How to deal with them. By Tracy J. Putnam, M.D. 12°, cloth, 168 pp., with 12 illustrations. Philadelphia: J. B. Lippincott Company, 1943. \$2.00.

This is a brief manual covering various types of convulsive diseases, particularly written for patients and their families and friends. There is a good discussion on seizures and their causes, with additional data on diagnosis and the principles involved in treatment. Excellent advice is given

certification. Health and accident policies depend to an appreciable extent, it would seem, on the knowledge and integrity of practicing physicians for actuarial soundness and for fairness in the disbursement of funds. Industrial organizations have used the insurance principle to provide various benefits for employees. Compensation statutes require medical judgments as bases to support legal judgments. It has been necessary to use the doctor's statement in an equitable enforcement of rationing while the nation is at war. As one contemplates the intricacies of modern society it is apparent that the end is not yet!

It is doubtful that the physician could or should avoid his function in verifying the existence and character of illness for legitimate ends. There is reason to believe that he should, in some instances, insist on more adequate compensation for the time spent in preparing factually accurate certificates. There is likewise reason to believe that some certificates could be shortened or modified without loss of pertinent information. To avoid them altogether does not seem possible.

While the nation is at war and struggling to use its manpower with maximum effectiveness, the need to limit absenteeism in industry has focused attention on the character of medical certificates. (Babey, A. M. Absenteeism. *J. A. M. A.* 122:395, 1943.) The certificate should be a reliable guide in releasing prompt financial assistance for the ill worker. An instance has been reported (Current Comment. *J. A. M. A.* 122:812, 1943) wherein a physician "issued a certificate to the effect that a worker was sick with gastroenteritis and was unable to work for a period of six days in the month of May, whereas investigation developed the fact that the person who submitted the certificate actually was working in another establishment and was attempting to obtain pay from two sources by requesting sick leave with pay from one of them."

From personal experience, a request for disability was recently honored on the basis of a physician's certificate stating that the worker was unable to perform even light work at the plant. The worker accepted his disability payments and spent several weeks pushing a wheelbarrow filled with rocks to landscape his residence property! It is true that the family physician risks an irate patient if the physician objects to signing whatever statement the patient requests. On the other hand, one may ask what degree of confidence and respect will the patient have in his doctor if the latter, unwittingly or not, falls in with such connivance?

There is a pitfall in another direction. In view of the marked emphasis given by industry and its advisers to matters of industrial hygiene, the worker with any complaint is likely to blame his working environment. He has had his attention called to this possibility, and it is altogether reasonable that wishful thinking will lead him to indict fumes, gases, vapors, dusts and the like. Actually many unskilled workers have no idea what, if any, exposure they have at their jobs. Such a worker in the role of patient may influence his family doctor to certify to a most astounding and untenable diagnosis. It would seem well to urge that physicians protect themselves against these pitfalls by using confirmatory sources of information. The plant and the plant physician are sources for checking facts. Other sources are the state and federal divisions of industrial hygiene. The exceptionally complete library on industrial health and hazards of the Division of Occupational Hygiene, Department of Labor and Industries, 23 Joy Street, Boston, is available to New England physicians.

Much medical certification is done well. These comments are made not in a spirit of censure but rather by way of directing attention to a potential danger to the good name of the profession. If we must sign certificates, may they invariably be as unbiased and factual as is humanly possible. Our jobs must be scientifically done. Industry depends on the physician for an answer to medical problems. Regardless of their difficulty there is no one who is better qualified to get the answers than is the physician. Therefore it is essential that the approach to these matters should be sound and of the highest ethical quality, so that traditions that have cast so much luster on medicine in the past shall continue to flourish in the future.

LEMUEL C. MCGEE, M.D., Medical Director
Hercules Powder Company

Wilmington, Delaware

TEST FOR HYPERSENSITIVITY TO SULFONAMIDES

To the Editor: In the important and comprehensive editorial, "Cutaneous Sulfonamide Hypersensitization," the May 18 issue of the *Journal* nothing is said about demonstrating hypersensitization. As the problem of sulfonamide hypersensitization is much broader than its cutaneous aspect, and since some of the general manifestations may be serious, even fatal to the patient, it would be helpful to have a satisfactory test of a patient's sulfonamide sensitivity. For this the use of the drug as a patch or intradermal has been unsatisfactory, since negative tests are frequent in fact, almost the rule. There is a test, however, simple and that is claimed by its originator to be positive in the great majority of patients. This consists in injecting intradermally a small amount of serum from a patient who is taking a sulfonamide drug (Lewitich, W. An intradermal test for recognition of hypersensitivity to sulfonamide drugs. *Bull. Johns Hopkins Hosp.* 74:26, 1943) with the production of a wheal if the patient tested is sensitive to the sulfonamide that the patient from whom serum was taken had been receiving. The test is said by the author to be highly specific and reliable in the diagnosis of sulfonamide sensitivity. If this is confirmed, it will be extremely useful in the clinic in the differential diagnosis of conditions simulating sulfonamide-sensitivity effects, particularly as a precautionary measure to prevent giving again a sulfonamide to a patient who previously had been sensitized to it.

HENRY A. CURRIE

20 Chapel Street
Brookline 46, Massachusetts

BOOK REVIEWS

Manual of Fractures: Treatment of external skeletal fixation. By C. M. Shaar, M.D.; and Frank P. Kreuz, Jr., M.D. cloth, 300 pp., with 148 illustrations. Philadelphia: W. B. Saunders Company, 1943. \$3.00.

This manual is the outgrowth of the authors' experience in the use of the Stader splint for 157 patients with various types of fractures. They give a concise and lucid description of the types of fractures best suited to this apparatus and the technique of its application, the postoperative care and hazards incident to its use. It has been found to be particularly useful in cases in which there are extensive burns or lacerations in the area of the fracture. This method of external skeletal fixation permits complete freedom of the joint which in turn lessens circulatory disturbances and muscle atrophy. Early use with rigid fixation also hastens union. In battle casualties its use facilitates early and evacuation from danger zones. The authors have observed no infection from the pins that hold the fragments. They advise gentle impaction with the turnbuckle bar after fracture is reduced. The treatment of different types of fractures, for example, that of the jaw, is taken up in detail. The apparatus, however, has been found most useful in fractures of the long bones. It has been used successfully in infected compound fractures and for fixation after grafts and arthrodesis. Chapters are appended on anesthesia in the treatment of fractures and on the roentgenographic aspects of fracture healing. The book is well illustrated with clear photographs.

Although this type of treatment of fractures will probably never become popular outside large hospitals, familiarity with such methods is desirable for all orthopedic and industrial surgeons. It is recommended as an interesting and useful book to those who are concerned with the treatment of fractures.

Geriatric Medicine: Diagnosis and management of diseases of the aging and in the aged. Edited by Edward J. Stieglitz, M.D. 8°, cloth. 887 pp., with 187 illustrations. Philadelphia and London: W. B. Saunders Company, 1943. \$1.50.

Geriatrics is becoming more and more a specialty of medicine since the number of older persons in this country is increasing.

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A PRELUDE TO ETHER ANESTHESIA*

WILLIAM W. FORD, M.D.

BALTIMORE

In the thirteenth century Hugh of Lucca employed the *spongia somnifera* or sleeping sponge to relieve the pain of surgical operations. He is said to have introduced it in about 1250, a recent date in the history of anesthetics. Hugh's famous disciple, Teodoric (Teodorico Borgognoni, 1205-1296), Bishop of Cervia, described the sponge in his surgical treatise of 1266 and has sometimes been credited with its invention. References to it occur in the *Antidotarium* of Nicholas of Salerno, said to have been compiled in the eleventh century and one of the early medical books to be printed in the rich topography of Nicholas Jensen at Venice in 1471. Some authorities maintain that the prescription for the sponge was derived from older formulas for anodyne applications to the temples for insomnia and was used to produce a form of local anesthesia, citing references to its appearance in the works of Copho, Gaddesden and others. The celebrated remedy was prepared as follows:

Take opium and juice of unripe mulberry, of hyoscyamus, of the juice of the leaves of the mandragora, of the juice of the wood ivy, of the juice of forest mulberry, of the seeds of lettuce, of the seed of the burdock, which has large and round apples, and of the water hemlock, each one ounce; mix the whole of these together in a brazen vessel, and then place a new sponge, and let the whole boil, and as long as the sun on dog days, till it (the sponge) consumes it all, and let it be boiled away in it. As often as there is need of it, place this same sponge into warm water for one hour, and let it be applied to the nostrils till he who is to be operated on has fallen asleep; and in this state let the operation be performed. When it is finished, in order to rouse him, place another dipped in vinegar, frequently to his nose, or let the juice of the roots of fenigreek be squirted into his nostrils. Presently he awakes.¹

The use of a pain-nullifying agent, however, goes back to remote antiquity, for ever since man has suffered he has sought a "drowsy syrup" that might bring relief. Six thousand years ago and more, mandragora was employed by the Babylonians; there are references to soporifics in the Talmud; and in the twenty-first verse of the second chapter of *Genesis* we read: "And the Lord God caused a deep sleep

to fall upon Adam, and he slept: and he took one of his ribs and closed up the flesh instead thereof." Indian hemp (*Cannabis indica*) was in all probability the drug used by the Egyptians when performing surgical operations, and it is claimed that Helen gave this same drug to Ulysses in the incident narrated in the *Odyssey*. The mention of bhang occurs in the *Arabian Nights*, and there is evidence that the Orientals and the Greeks were quite familiar with the narcotic properties of opium, henbane, dewberry, lettuce and hemlock.

Inhaling the vapor of bhang for anesthetic purposes is mentioned in the writings of Hippocrates about 400 B.C. and later references to some form of narcosis are to be found in the works of Pliny, Dioscorides, Paulus Aegineta, Celsus and Avicenna. Pliny the Elder (23-79 A.D.) described mandragora and spoke of its soporific powers. It was also recommended as a surgical sleeping draught by Dioscorides† and Apuleius.

About 165 A.D. the Greek physician and philosopher Galen employed as an anesthetic for the removal of teeth an application of "pirethrin root and strong vinegar, from the action of which, the remaining teeth may be preserved by covering them with a layer of wax. At the expiration of an hour, the tooth becomes so loosened, as to be easily removed."²

Hao Tho, Chinese court physician at the beginning of the third century, operated on his patients while they were under the influence of a preparation of the hemp plant sometimes called "may-yo" and similar to the hashish of the Arabs.

The Peruvian Indians found a remedy in coca leaves, chewing them and swallowing the saliva. Persisting in the habit, they were apparently able to build up a considerable immunity to pain. In 1911, H. J. Mozans³ cited a modern instance of a *coquero* (one habitually chewing coca leaves) who was run over by a car. His foot was taken off in the accident, but he gave little or no evidence of suffering. The shamans or priests of old Peru also chewed

*This article forms the opening chapter of a forthcoming publication, *diagn. Thomas Green Morton and the Discovery of Surgical Anesthesia*, by the late William W. Ford, M.D., D.F.H., emeritus professor of otolaryngology, School of Hygiene and Public Health, Johns Hopkins University.

†Dioscorides was the first to refer to the use of mandragora wine as an anesthetic, and his formula was successfully tested by Richardson.²²

regarding various drugs, and this part of the book is distinctly valuable to physicians. The final chapter deals with legal problems connected with epilepsy, and there is an up-to-date reference to the current literature in an adequate bibliography.

This is a book that may be put in the hands of the more thoughtful patient and will be of value to a considerable proportion of practitioners who occasionally have to make decisions in regard to epilepsy.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Backache and Sciatic Neuritis: Back injuries—deformities—diseases—disabilities. By Philip Lewin, M.D., associate professor of bone and joint surgery, Northwestern University Medical School, attending orthopedic surgeon, Michael Reese Hospital and Cook County Hospital, professor of orthopedic surgery, Cook County Graduate School of Medicine, Chicago, and lieutenant colonel, Medical Corps, United States Army. With line drawings by Harold Laufman, M.D., instructor in surgery, Northwestern University Medical School, Chicago, and captain, Medical Corps, United States Army. 8°, cloth, 745 pp., with 235 illustrations. Philadelphia: Lea and Febiger, 1943. \$10.00.

This new book is a comprehensive treatise on diseases and injuries of the back. Emphasis is placed on diagnosis and treatment; the medicolegal, industrial and military aspects, are also discussed.

Pathology and Therapy of Rheumatic Fever. By Leopold Lichtwitz, M.D. With a foreword by William J. Maloney, M.D., LL.D., F.R.S. (Edin.), consulting neurologist to the City Hospital, New York City. Edited by Major William Chester, M.C. 8°, cloth, 211 pp., with 69 illustrations and 11 tables. New York: Grune and Stratton, 1944. \$4.75.

This monograph discusses rheumatic fever in all its acute and chronic aspects.

Internal Medicine in General Practice. By Robert P. McCombs, M.D., lieutenant, Medical Corps, United States Naval Reserve. 8°, cloth, 694 pp., with 114 illustrations. Philadelphia: W. B. Saunders Company, 1943. \$7.00.

This new manual on internal medicine is written especially for practitioners and students, and the field of diagnosis and treatment is especially emphasized. All the newer methods and mechanical aids in diagnosis have been included.

The Youngest of the Family: His care and Training. By Joseph Garland, M.D., physician to the Children's Medical Department, Massachusetts General Hospital, consulting pediatrician, Massachusetts Eye and Ear Infirmary, and instructor in pediatrics, Harvard Medical School. Revised edition. 12°, cloth, 182 pp., with 11 illustrations. Cambridge, Massachusetts: Harvard University Press, 1943. \$2.00.

This is a revision of a manual first published in 1932. It has been written to meet the exigencies of wartime. Because of the difficulty of obtaining many of the luxuries that once seemed indispensable in the care of the baby, instructions have been reduced to the simplest terms. Dr. Garland is a well-known pediatrician, and this revised edition should prove to be even more useful and valuable to the mother than the former edition.

Medical Genetics and Eugenics. Volume 2. By R. Ruggles Gates, Ph.D., D.Sc., LL.D., F.R.S., Marine Biological Laboratory, Woods Hole, Massachusetts; Laurence H. Snyder, B.S. M.S., Sc.D. professor of medical genetics, Ohio State University; and Earnest A. Hooton, Ph.D., Sc.D., Department of Anthropology, Harvard University. 8°, cloth, 60 pp., with 13 illustrations. Philadelphia: Woman's Medical College of Pennsylvania, 1943. \$1.00.

The present volume includes lectures given before a audience at the College of Physicians, Philadelphia. They have to do with the subject of heredity.

Fractures and Dislocations for Practitioners. By Edgar Geckeler, M.D. Third edition. 8°, cloth, 361 pp., with illustrations. Baltimore: The Williams and Wilkins Company, 1943. \$4.50.

This book was first published in 1937. The third edition has been revised to include sections on emergency and fracture wounds, particularly vital at the present time. New procedures have been simplified and considerable attention has been given to chemotherapy in the treatment of traumatic wounds. Débridement in the treatment of compound fractures is described so that the physician can perform the operation without delay if an experienced surgeon is not available. The manual is primarily written for the general practitioner who may be required to treat traumatic injuries in the absence of a competent surgeon.

Prelude to Sanity. By S. Greiner. 8°, cloth, 164 pp. Lauderdale, Florida: Master Publications, 1943. \$3.00.

It is the author's contention that, contrary to common psychiatric belief, schizophrenia does not constitute a clinical but a generic phenomenon.

Ship's Doctor. By Rufus W. Hooker, M.D. 8°, cloth, 272 pp. New York: Whittlesey House, 1943. \$2.50.

This is the autobiography of a physician who for four years followed the practice of medicine at sea, sailing a million miles in that time. The book is written in a narrative style and relates many experiences of Dr. Hooker in varying situations, ranging from the urgent call to SOS to conveying the wounded from Pearl Harbor and the Philippines.

The 1943 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D., orthopedic surgeon, the Massachusetts Women's Hospital and Beth Israel Hospital, Boston. 12°, cloth, 440 pp., with 306 illustrations. Chicago: The Year Book Publishers, 1943. \$3.00.

This volume provides a summary of progress for the year in the fields of orthopedic surgery and of industrial medicine and surgery. The material is well selected and printed in excellent type on a good grade of paper.

Nascent Endocrine Therapy. By John F. Ritter, M.D. 8°, cloth, 317 pp. Caldwell, Idaho: The Caxton Printers, Limited, 1940. \$5.00.

In this book the author describes his treatment of essential hypertension.

Medical Advice from a Backblock Hospital. By G. M. Smith, M.B., Ch. B., F.R.C.S.E. With articles and notes by A. Bedgood, Vernon Brown, F. Cook, L. M. Copley, N. Gilchrist, E. Harwood, A. Kernihan, W. H. Kirkpatrick, E. Tait, H. Maxwell and Barbara Orr. Second edition. 8°, paper, 96 pp. Wellington, New Zealand: Progressive Publishing Society, 1943. 1 shilling.

This work is a description and an explanation of the Hologanga Co-operative Clinic Medical Service, located in New Zealand. The first edition was published in March, 1942, and the second edition affords the author an opportunity to reply to the criticism and to answer his critics. The principal part of the pamphlet is a manual of domestic medicine to which are added replies to critics on social medicine among the Maoris.

Child Welfare Handbook: A guide to health and social service. Edited by Beatrice S. Stone. 8°, paper, 58 pp. Boston: Publications Committee of the Massachusetts Child Council, Incorporated, 1943. 25 cents.

This pamphlet is fundamentally a directory of all organizations in Massachusetts having to do with child welfare. It is an essential reference source of information concerning the subject.

the chemistry of the various substances called "ether" was not always well understood. Accurate directions for making it were probably first given in the *Pharmacopoeia* published by the Massachusetts Medical Society in 1808 and prepared for the Society by Dr. Jacob Bigelow and Dr. James Jackson. But it was not until 1830 that methods of preparing ether were given *in extenso* and became widely available in America. In that year the *Pharmacopoeia of the United States* gave a complete account of the preparation of its listed drugs, and the chemistry of the different ethers was further cleared up when Daniel Smith¹² published a comprehensive paper in the *Journal of the Philadelphia College of Pharmacy* in 1832–1833. He described over fourteen chemical compounds called "ether," among them a variety of chloric ether (later known as chloroform), sulfuric ether and oil of wine.*

Additional references to ether appeared in Pereira's widely read *Elements of Materia Medica*,¹³ published in 1839—three years before the first operation under ether narcosis was to be performed by the young country practitioner at Jefferson, Georgia. Earlier and painstaking investigation, which Sir Humphry Davy styled "the pathetic quest for oxygen," terminated brilliantly with the discovery of several gases in the second half of the eighteenth century, and the Chemical Age was firmly established. The discovery of carbon dioxide by the Scottish chemist Joseph Black, in 1757, was followed by the discovery within the next eighteen years of hydrogen by Cavendish, nitrogen by Rutherford and oxygen by Priestley, the Swedish investigator Scheele and Lavoisier. Preceding his discovery of "dephlogisticated air," as he called oxygen in accordance with Stahl's doctrine,† Joseph Priestley had discovered nitrous oxide in 1772. In 1775 oxygen, which John Mayow had come so near discovering in the seventeenth century, was once more isolated and clearly defined by Antoine-Laurent Lavoisier, and the phlogistic doctrine, long confusing and hampering chemists, was overthrown by this distinguished worker.

Medical practice was soon influenced by the various discoveries, particularly that of oxygen, physicians were carried away by their imaginations to the extent of attributing diseases either to lack or excess of oxygen, or to some fine-spun modifications of this theory," as Garrison¹⁴ has said.

A pioneer in the use of gases in medicine and contributing indirectly to the advancement of

anesthesia was Dr. Thomas Beddoes, who founded a Pneumatic Institute at Clifton Hotwells near Bristol, England, in 1798. Here bodily and mental ills were treated by the inhalation of gases, and a sort of inhalation therapy developed and became extremely popular for a time.

The noted James Watt, in addition to collaborating with Beddoes in the publication of *Factitious Airs*, which related to the pneumatic methods, had constructed the apparatus at the institute, and Humphry Davy was Beddoes's chief assistant. In 1799 Davy¹⁵ published the results of his experiments with nitrous oxide gas, which he had discovered to be an anesthetic while inhaling it to relieve an aching tooth. A little later he gave a series of popular lectures, followed by demonstrations of nitrous oxide, calling it "laughing gas." In 1800 further demonstrations of the gas were given by William Allen, the lecturer on chemistry at Guy's Hospital in London.

A man of wide interests and extensive acquaintance, Dr. Beddoes's work at Clifton, which the youthful Davy described as "the loveliest spot in the world," attracted the attention of Erasmus Darwin, Thomas Wedgewood, Wordsworth, Coleridge, Southey and many others. Both Southey and Coleridge were among the first to inhale nitrous oxide after Davy's successful experiments, Coleridge writing a glowing account of his sensations. But after a few years the initial enthusiasm began to decline, medical opinion altered, and there were many rumors concerning patients who had been troubled with dizziness, lowered pulse and other unfavorable symptoms as a result of pneumatic methods. Several years before his death in 1808, Beddoes, disillusioned, his theories having encountered strong opposition on all sides, converted the institute into a hospital where the usual forms of treatment were adopted, Humphry Davy meanwhile dropping his own investigation of nitrous oxide gas to win many laurels in other fields.

In about 1784 James Moore revived anesthesia by compression. The principal nerves and vessels of the neck were compressed to produce local anesthesia or insensibility. But after some fatal results this practice was soon discontinued.

Shortly before the French Revolution, Frederick Anton Mesmer employed animal magnetism or "magnetic emanations" to produce insensibility to pain, his armamentarium including a lilac robe (which he always wore at his hypnotic séances), a harmonica, a magnetized wand and later the *baquet* or wooden tub, containing a series of bottles "charged with animal magnetism." Discredited in Vienna, Mesmer had settled in Paris in 1786. Here he was also rebuffed, but not before he had enjoyed a period of extraordinary success and prosperity, being acclaimed by members of the French Court and other celebrities. He failed in all his efforts to obtain scientific recognition, however, and at the outbreak

*Until the early 1850's ether was produced by the open fire, intermittent distillation method. This method was not only dangerous from the standpoint of fire hazard but involved the problem of selecting the correct proportion of the distillate to be employed for anesthesia. In 1856 an important contribution was made by Edward R. Squibb, then assistant director at the United States Naval Laboratory. Experienced in the manufacture of ether for some years past, he had developed a method of making the drug by continuous steam heat through lead coils, and in an article entitled "Apparatus for the preparation of ether by steam," published in the September, 1856, issue of the *American Journal of Pharmacy*, gave a detailed report of his new, and revolutionary method.

†The principle of inflammability supposedly existing in combustible bodies. The theory was that when matter burns it gives off a hypothetical substance, "phlogiston."

the leaves and applied the spittle to the wounds of their surgical patients. From the active principle contained in the leaves of *Erythroxylon coca* the alkaloid cocaine was to be produced in the nineteenth century.

Compression effected by mechanical means and continued a sufficient length of time to cause numbness in that part of the body to be operated on, was first practiced by the Egyptians and has been reintroduced by surgeons at different periods.

Following Theodoric, Guy de Chauliac (1300-1368), the great surgeon of the Middle Ages, is the only medical historian of importance to mention or describe the "sleeping sponge."⁴ In the medical writings of the period there are other references to the use of narcotics, chiefly opium, but at the same time the danger of asphyxia, congestions and even death as a result was emphasized. Unquestionably this did much to retard the practice of any extensive drugging in the treatment of patients. It is stated, however, that criminals of the fourteenth, fifteenth and sixteenth centuries, when facing execution or prolonged forms of torture, frequently had some narcotic dose administered by a compassionate jailer.

More than one reference to anesthesia has occurred in literature while the actual use of it was declining. Boccaccio, Shakespeare, Marlowe and Middleton all mention narcotics. The well-worn quotation:

I'll imitate the pities of old surgeons
To this lost limb, who, ere they show their art,
Cast one asleep, then cut the diseased part.

taken from Middleton's *Women Beware Women*, furnishes perhaps the best example.

* * *

In the middle of the sixteenth century the skillful hands of Ambroise Paré (1510-1590) lessened the supreme torments of surgery by the application of ligatures and simple dressings in place of boiling oil or cauterization with red-hot irons—the usual treatment for wounds and the stumps of amputated limbs. Following on his chance discovery, as military surgeon before Turin, that gunshot wounds were not "poisonous," Paré opposed the doctrines of his contemporaries and conducted a spirited campaign for the adoption of soothing methods in wound treatment, but the use of the sleeping potion or "sponge" was apparently unknown to him. And in the seventeenth century, during which medical history was enriched by an imposing catalogue of names beginning with that of William Harvey (1578-1657) and the dignity of medicine was so ably portrayed in the canvases of some of the great Dutch painters, including the "Anatomies" of Adriaen Backer and Johan Van Neck, the employment of any pain-relieving agent was forgotten or almost wholly disregarded.

In 1730 the chemist Frobenius described sulfuric ether in the *Philosophical Transactions* of the Royal Society at London,⁵ designating it "spiritus vitæ æthereus." The preparation of ether by the action of sulfuric acid on alcohol had been known since the thirteenth century. Raymond Lully (1235-1315), philosopher and alchemist of prominence, was apparently the first to discover it. The drug was then referred to as "sweet vitriol" or "*oleum dulce vitrioli*." In 1540 ether was rediscovered and its properties described by Valerius Cordus (1515-1544), a young apothecary and a student under Paracelsus, who had once happened on ether himself, it is stated, trying the effects of it on chickens. More than a century later "sweet vitriol" was also mentioned by Sir Isaac Newton, Godfrey and Boyle.

During the eighteenth century the medicinal employment of ether was alluded to by such prominent physicians as Hoffmann (Hoffmann's anodyne), Cullen, Alston, Lewis and the Monros. In 1795 Richard Pearson recommended the inhalation of ether in treating phthisis or pneumonia, directing that the patient "pour one or two teaspoonfuls of pure vitriolic ether, or ether impregnated with icuta . . . into a teacup or wineglass and inhale the same three, four or five times a day."⁶ Several communications from Pearson are included in *Facitious Airs*,⁷ the essays of James Watt and Dr. Beddoes, published at Bristol, England, in 1795, and printed in the *Annals of Medicine* the following year. One of Pearson's communications refers to a letter from Dr. Thornton describing the inhalation of sulfuric ether in treating catarrh, where the patient, much relieved, fell into a deep slumber.

In 1815 Nysten, in a dictionary of medical sciences,⁸ spoke of ether as familiarly known for mitigating the pains of colic and other minor ills, and described apparatus or methods for inhaling it.

Michael Faraday, in 1818, published the following in the *Quarterly Journal of Science and the Arts*: "When the vapour of ether is mixed with common air and inhaled, it produces effects very similar to those occasioned by nitrous oxide. By the incautious breathing of ether vapour, a man was thrown into a lethargic condition which, with a few interruptions, lasted for thirty hours."

Dr. John Collins Warren spoke of resorting to the inhalation of ether as early as 1805 in order to relieve a patient dying of pulmonary tuberculosis.⁹ In 1832 Daniel Drake listed ether among the remedies to be taken internally for cholera.¹⁰ Franklin Bache, in 1833, collaborating in the preparation of the massive *United States Dispensatory* (first edition) gave a description of the chemical properties of the drug and referred to its medicinal uses.¹¹ Other American authorities mentioning ether during the decade of 1822-1832 included Godman, Mitchell and Professor Samuel Jackson. In considering the early references, however, it should be remembered

of the Revolution left Paris and lived in retirement for some years before his death, which occurred in 1815. But mesmerism, invading surgery in the nineteenth century, was to have such disciples as Braid, the outstanding pioneer of scientific hypnosis and originator of "Braidism," Elliotson and Esdaile. John Elliotson, a friend of Thackeray's, to whom the novelist dedicated his *Pendennis*, performed the first surgical operations in about 1840 on patients who had been hypnotized, claiming success. In 1843 he published a pamphlet, *Numerous Cases of Surgical Operations without Pain in the Mesmeric State*, which soon provoked dispute and led to his resignation as president of the Royal Medical and Chirurgical Society, as a professor of practice in the University of London and to his withdrawal from other offices. James Esdaile fared much better in the Indian Medical Service, and his operative work among the Hindus, which he began in 1845, attracted attention for some time, although the general verdict of the Western scientific world was distinctly unfavorable.

In 1808, Frederick Wilhelm Sertürner, a German apothecary, extracted morphine from crude opium. Publishing the results of long experiment, he received honorary degrees from the Universities of Paris, St. Petersburg and Berlin, among others. In 1831, he was awarded a Montyon prize of 2000 francs for his discovery. Nevertheless, the conquest of pain in surgery was generally regarded as a remote possibility at this time, and Sertürner, becoming embittered by certain manifestations of professional jealousy, engaged at length in the study and improvement of firearms.

Severino had produced local anesthesia with snow and ice in 1640. At the battle of Eylau in February, 1807, Napoleon's surgeon-in-chief, Dominique Jean Larrey, who on occasion performed two hundred amputations in twenty-four hours, observed that wounded men half frozen from the cold experienced little pain when operated on. Larrey's discovery led to refrigeration anesthesia, which was shown to have so many undesirable features that it was soon abandoned. Later it was reintroduced.

In 1824 a young English physician, Henry Hill Hickman, performed a number of operations on animals, using carbon dioxide as an anesthetic. Hickman, it is said, first became interested in gases as a result of practicing for a time at Shiffnal, the birthplace of Dr. Beddoes. Returning to his native Ludlow in Shropshire, Hickman studied the work of Priestley, Davy and Faraday and conducted a series of experiments. Encouraged by the apparent success of his efforts, he went on to employ nitrous oxide when performing various operations on dogs, chickens and cats, and at about this time attempted to interest the Royal Society in his work. Writing to a friend, T. A. Knight, a botanist and member of the society, he gave a detailed report of his experiments, making the request that it be sub-

mitted to the proper authorities. But Knight, although at once interesting himself in the matter, was unable to help him. Both Sir Humphry Davy, then president of the Royal Society, and Michael Faraday were engaged in other absorbing problems, and Hickman's report was never even read before a committee.

Hickman, entertaining high hopes of being able to operate on his own patients under anesthesia, was not ready to accept defeat and printed a public letter. When this was ignored he presented a memorial to King Charles X of France in 1828, containing the statement: "It appears demonstrable that the hitherto most agonizing dangerous and delicate surgical operations may now be performed, with perfect safety, and exemption from pain, on bruta animals in a state of suspended animation" But the French were not interested after the Royal Academy of Medicine, with the possible exception of Dominique Larrey, failed to find anything of importance in Hickman's claims. Doomed to disappointment, Hickman could only continue his work alone. He died in 1830 at the age of twenty-nine, and more than a decade was to pass before the discovery of surgical anesthesia.

Samuel Guthrie, of Sackett's Harbor, New York, made chloroform in 1831 by distilling alcohol with chlorinated lime. In that same year chloroform was discovered independently by Soubeiran¹⁷ in France, and Leibig¹⁸ in Germany. It was first used medicinally as a solution of chloric ether, and regarded as a particularly pleasant intoxicant. "During the last six months, a great number of persons have drunk of the solution . . . in my laboratory," Guthrie wrote, "not only freely but frequently to the point of intoxication . . . it has appeared to be singularly grateful, both to the palate and stomach, producing promptly a lively flow of animal spirits, and consequent loquacity; and leaving, after its operation, little of that depression consequent to the use of ardent spirits."¹⁹ In July, 1832, Daniel Smith, in classifying it among the ethers, observed: "The action of this ether on the living system is interesting and may hereafter render it an object of importance in commerce. Its flavor is delicious, and its intoxicating qualities equal to or surpassing those of alcohol."¹² Jean-Baptiste Dumas analyzed the solution in 1834 and gave it the name of chloroform, but its anesthetic qualities were not to be recognized until James Y. Simpson introduced it in childbirth some thirteen years later.

The picture, then, was not too bright. Surgical technics had improved since Paré, but human suffering was much the same. "A humiliating spectacle of the futility of science," John Hunter declared in the eighteenth century, and in the nineteenth Charles Darwin, writing his *Autobiographical Recollections*, recorded: "I also attended on two occasions the operating theatre in the hospital at Edinburgh and saw two very bad operations, one on a child.

e instructor. In the last analysis the material is ing presented to the student for purposes of instruction, and if he gains nothing from it, it should be revised to the point where it is beneficial.

The next question is whether it is better to use typewritten material or that turned out by any of the semimechanical lettering guides now in use. Typewritten material is the poorest of all from the standpoint of projection on a screen because of the plain body of the characters and the ragged appearance of the type when enlarged on the screen. It is generally agreed that semimechanically lettered charts of tabulated material are much more easily read and present a much neater appearance. This is particularly important when material is to be presented at a medical meeting, because every speaker falls in the estimation of his audience if his lantern slides are poor.

When tabulated material is being prepared, more pleasing results will be gained if it is kept within proportions of the lantern slide, which is $3\frac{1}{4}$ by 4 inches. This produces the maximum size of letters on the screen for any given projection distance and ensures a minimum of wasted space.

Another subject of controversy has frequently been the number of x-ray films or ordinary photographs that can be reproduced on a single lantern slide. Here again, it depends somewhat on the subject whether more than two images can be placed on one slide and projected so that the entire audience can see the subject plainly. A single tiny spot on a chest plate reproduced in four films on one lantern slide is apt to show up poorly because of the small size of the projected image. On the other hand, details that are relatively large in a single film or photograph show up well in a number of images on one slide.

Motion pictures have come into great prominence during the last few years as a medium of teaching medicine. An enormous number of films have been made by many persons — some of them good and some worthless, not from the standpoint of poor photography but from that of scene length and continuity. This defect is caused by lack of preparation before the film is made. A good teaching film must be prepared in the form of a scenario or scene schedule. If it is an operative film, the photographer should see a similar operation before attempting to produce a motion picture, in order that he may know what to expect during the actual making of the film.

It is not infrequent that some interesting material is discovered during an operation and someone conceives the idea of having a motion picture made of it on the spur of the moment. Often after the film is made, it is never used and is forgotten, but if used by someone, it is found that the film was started in the middle of the operation. There is no preliminary matter to explain what went on before and no follow-up to show the end result. In general,

films of this nature have absolutely no reason for being.

The preparation of a properly made medical teaching film begins with a conference between the instructor and the photographer, at which time a rough outline of what should be covered is laid out, and from this a taking schedule or scenario is made up. At that time the photographer and the instructor find out what each will need for material and what material will be required for each scene. They decide how much should be included in the scene, and whether to employ a close-up view or a long shot, and attend to the thousand and one details that must be settled before a single foot of film is run through the camera. In this way a minimum of material is wasted, the work proceeds more rapidly, and the end result is usually satisfactory and does not require additional scenes to be supplied at a later date.

When using color film in motion pictures, it is desirable that all the film be processed at one time, because there are minor variations in color in different processing solutions. For this reason the scene schedule should be complete before the film is processed. The use of color in motion pictures has been greatly accelerated in the last three years. Many medical subjects are far more realistic when done in color. Others can of course be done in black and white, but color is here to stay and wider use should be made of it whenever possible.

There has been much controversy over the length of a teaching film. Some experiences lead one to believe that a medical student cannot possibly stay awake through a film that lasts over ten minutes. Actually, if a film is presented in an interesting manner, there is little difficulty in keeping his attention. Thirty to forty minutes of running time seems to be the average period during which his interest can be held. Students frequently criticize motion pictures showing treatment because the latter is made to appear much too easy or simple. One of the reasons for this is that the average motion picture of treatment procedure shows only the high lights, omitting the minor motions and the preparation for treatment. On the other hand, if a film is to show all the preparation, treatment and after-care, great pains must be taken so that it will not drag, for the student frequently loses interest if this occurs.

Four or five years ago, a noted pediatrician and a clinical photographer successfully worked out a method of presentation of motion pictures in conjunction with one of the former's lectures. The projection material consisted of a series of short films pertinent to the subject of the lecture, which were connected by short pieces of blank film. The running of each section required from 30 to 60 seconds. The instructor proceeded with his lecture, and at certain points he paused and a section of the film was shown. As soon as this particular section

AIDS TO VISUAL EDUCATION IN MEDICINE

F. R. HARDING*

BOSTON

THERE is greater need for a wide use of visual aids in teaching medical subjects at this time than there has been for many years. With such a large number of instructors now in the armed forces, it becomes necessary to use every possible aid in teaching.

Visual aids may take several forms. Large charts, photographs, lantern slides and motion pictures are all most necessary. Each of these forms has its own particular function to fulfill. It should be borne in mind that a photograph can tell a student more than can many pages of printed matter. Tests conducted by the United States Bureau of Education¹ have definitely proved that students learn more in a shorter time through pictures than they do from printed matter or the spoken word. With the greatly concentrated medical teaching program now in progress, it seems necessary to use all these visual aids to the largest possible extent.

Large charts are frequently advantageous in presenting material in tabulated form. They may be hand-lettered on large sheets of paper and placed on an easel before the students. These charts are of particular value if the students are required to copy the material in notebooks. The chart is usually left on the easel for a length of time sufficient to allow the slowest student to copy the material. Sufficient classroom lights should be on to enable the students to see their notebooks. Tests should be conducted to make sure that too much material is not placed on the charts. The material should be condensed as much as possible, bearing in mind that students absorb more readily two charts with ten lines on each than one chart with twenty lines. All charts must be so constructed that they can be easily read by students in the back rows.

Photographs can frequently be used to their best advantage in bedside teaching by showing the patient before and after treatment. They may also be enlarged and used as an exhibit. An exhibit of this kind is of no value unless a printed description accompanies each photograph and the students are given sufficient time in which to study it thoroughly. A place for a permanent exhibit can sometimes be arranged, with great benefit to the students.

The primary use of photographs is in the clinical record. It must always be borne in mind that the medical student rarely has a chance to see more than a small percentage of the patients both before and after they have been treated. The more complete the photographic record, the more valuable it will be for the purpose of study.

*Director of photography, Children's Hospital.

Lantern slides are invaluable for covering a complete topic. They have been used and misused for many years, and there is a great deal of controversy over the best method of displaying them. It is generally understood that about forty lantern slides an hour is the maximum that can be taken in by students. This allows an average of somewhat over a minute for discussion of each lantern slide. If it is thought that more slides than this must be used, it is suggested that the slides be re-examined with a view toward discarding those that are of least importance. If more than forty lantern slides an hour are projected, the effect is most disconcerting to the student, sometimes to such a point that he gains nothing from the material. Many slides contain tabulated material — sometimes large quantities of it. From the student's point of view, this is undesirable, for two reasons. First, he is discouraged by a large mass of material and frequently does not bother to read it all. Second, large masses of printed material reproduced on a lantern slide are extremely small even when projected, and if the lecture room is large, those at the rear of the room may be unable to read what is on the screen. Some years ago the members of the Mayo Clinic² after considerable study reached the conclusion that for general use under varying conditions, fifteen typed lines of tabulated material is the maximum that should appear on a slide. This amount can be somewhat increased, probably to twenty lines, if the material is made with lettering guides instead of on a typewriter. Because of unknown projection conditions, such as the distance from the projector to the screen and the size of the screen in relation to that of the room, lantern slides must be so made that they will give the desired message regardless of local conditions.

Sometimes large quantities of material are necessarily projected on the screen to show the pattern or course of some particular subject; this does no harm. At other times a large amount of material is prepared in the form of a lantern slide as a guide to the lecturer. This is rather unfair to the student because the material must be read by the instructor and could be included in his text. If typed tabulated material is divided into sections with India ink, it becomes much easier to follow on the screen. Frequently masses of material can be broken down into more than one lantern slide with great benefit to the student. The instructor often loses sight of the fact that if his material is not good or is poorly presented, the student gains little or nothing from the time and effort that have been devoted to it by

material will undoubtedly be projected and that it must be readable from the back of the hall.

For deciding on the proper size of screen, a good rule is that the width of the screen should be one sixth of the distance from the screen to the back row of seats. This rule is adequate, and works well when the first row of seats is ten feet or more from the screen. If the screen must be nearer the audience than this, it should be slightly smaller so that the projected image will not appear excessively magnified or distorted.

The projection screen should be chosen with regard to the shape of the auditorium. If most of the seats come within a viewing angle of 25° , as is true in the average lecture hall, a beaded screen will produce the greatest brightness. If the room has small depth but great width, a white screen will produce the best brightness for the majority of the audience. In the latter case vision from an angle of greater than 45° is sure to be distorted.

Pertinent data covering the focal-length of the lens, the distance from the lens to the screen and the size of the image are given in Figure 1. These

are based on a 3-inch opening in the slide. Since some slides utilize the entire effective width ($3\frac{3}{4}$ inches), the screen must be large enough to care for these slides also.

Projection screens should be protected from dust when not in use, and the lens mirrors and condensers should be kept spotlessly clean. When projectors equipped with Mazda lamps are used, old, blackened lamps are a prolific cause of poor illumination.

300 Longwood Avenue

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MULTIPLE EXTRAGENITAL GIANT CHANCRES*

Report of a Case.

WALTER F. LEVER, M.D.†

BOSTON

RECENTLY a patient with three large ulcerated extragenital chancres was seen at the Massachusetts General Hospital. Two chancres were located on the chin and one in the left inguinal region. A report of this case is submitted not only because of the unusual size of the chancres but also in order to emphasize the importance of considering a diagnosis of primary syphilis in dealing with ulcerated lesions of the skin.

CASE REPORT

A 28-year-old woman first noticed two small papular lesions, one on each side of the chin, on June 10, 1943. One week later, a similar papule developed in the left groin. The three lesions gradually increased in size and became slightly raised and covered with heavy, dark-brown crusts. Two weeks after onset, the right submaxillary lymph nodes became enlarged and so painful that the patient lost much sleep. The lesions themselves were neither painful nor tender.

On July 10, one month after onset, the patient was seen at the Massachusetts General Hospital. The lesions were covered with heavy, oyster shell-like crusts. Each of those on the chin showed, after removal of the crusts, a central ulceration surrounded by a bright-red, slightly raised margin (Fig. 1). The larger lesion, on the right side, measured 3.5 by 4.4 cm., and its central ulceration 1.6 by 2.8 cm. The

lesion on the left side measured 1.5 by 1.5 cm., and its central ulceration 0.5 by 0.6 cm. Palpation of the lesions revealed distinct induration of the margins as well as of the bases of the ulcers. Both showed a granulating base covered by a grayish-green membrane of necrotic tissue. The edges of the ulcers were slightly serpiginous and overhanging. There was profuse secretion of a clear, serous exudate in amounts large enough to cause occasional dripping from the lesions. The right submaxillary lymph nodes showed moderate enlargement and considerable tenderness. The left submaxillary, anterior cervical, submental and hyoid lymph nodes were slightly enlarged but not tender.

The lesion in the left inguinal region presented, after removal of the overlying crust, a narrow, cleftlike central ulceration surrounded by a wide area of erosion (Fig. 2). The entire lesion measured 5.5 by 1.5 cm., and the ulcer 1.7 by 0.2 cm. There were the same induration and the same serous secretion as those observed with the lesions of the chin. The left inguinal lymph nodes were moderately enlarged but not tender.

Aside from the three ulcers the skin was normal. There were no lesions on the visible mucous membranes, and on examination by speculum the vaginal mucosa and cervix were found to be free from lesions.

Darkfield examination revealed in each of the three lesions numerous spirochetes whose characteristics conformed to those of *Treponema pallidum*. Aerobic and anaerobic cultures showed only a few colonies of *Staphylococcus albus*. Reactions to both a Hinton and a Wassermann test were positive. Intracutaneous tests for chancroid and lymphopathia venereum were negative.

To avoid a Herxheimer reaction, arsenicals were at first withheld and treatment was inaugurated with five injections of water-soluble bismuth sodium tartrate, 0.2 gm. being given on alternate days. On the day following the first injection, a generalized macular eruption appeared on the skin. A diagnosis of secondary syphilis was made.

*From the Departments of Dermatology and Syphilology, Massachusetts General Hospital.

†Assistant in dermatology, Harvard Medical School; assistant in dermatology, Massachusetts General Hospital, junior associate in dermatology, Peter Bent Brigham Hospital.

had been run through the projector, the latter was stopped and the lecture proceeded until the next of what were called "punch points" was presented. In this way the student was able to see the actual characteristics of the subject under discussion at the time when the symptoms and treatment were fresh in his mind.

If the instructor depends on living patients to illustrate his lecture, he frequently finds that, when the lecture period comes around, he has no patient with the particular feature that he is going to discuss. By using motion pictures the subject is always there, rolled on a little reel and sealed in a tin. A much wider use of motion pictures could be made

of a patient that could not be recorded photographically was the plantar aspect of the feet when bearing weight. It is now possible to do this quite successfully.⁶ The required apparatus is simple and easily constructed. It opens a new field to the orthopedist for the photographic and visual record of patients with foot deformities.

Photography in the operating room is of great value in visual education, particularly when teaching time is so precious and students have little opportunity to observe operations. The photographic problems involved do not properly concern the instructor, and they vary in every hospital. Most of these have been solved, and a much greater

Focus of Lens in Inches	DISTANCE FROM SCREEN, IN FEET															
	4	5	6	8	10	15	20	25	30	40	50	60	70	80	90	100
4¼	2.6	3.3	4.0	5.4	6.8	10.3	13.8									
5½	1.9	2.2	3.0	4.1	5.2	7.9	10.6	13.4								
6½	1.6	2.0	2.5	3.4	4.4	6.7	9.0	11.3	13.6							
8	1.3	1.6	2.0	2.7	3.5	5.4	7.2	9.1	11.0	14.8						
8½	1.2	1.5	1.9	2.6	3.3	5.1	6.8	8.6	10.3	13.9						
10		1.3	1.6	2.2	2.8	4.2	5.8	7.3	8.8	11.8	14.8					
12			1.3	1.8	2.3	3.5	4.8	6.0	7.3	9.8	12.3	14.8				
14			1.0	1.5	1.9	3.0	4.0	5.1	6.2	8.3	10.5	12.6	14.8			
16				1.3	1.6	2.6	3.5	4.5	5.4	7.3	9.1	11.0	12.9	14.8		
18				1.1	1.4	2.3	3.1	3.9	4.8	6.4	8.1	9.7	11.4	13.1	14.7	
20	Width of Screen Picture in Feet					2.0	2.8	3.5	4.3	5.7	7.3	8.8	10.2	11.8	13.2	14.8
22						1.8	2.5	3.2	3.8	5.2	6.6	7.9	9.3	10.7	12.0	13.4
24						1.6	2.2	2.9	3.5	4.7	6.0	7.2	8.5	9.7	11.0	12.3

Courtesy of the Spencer Lens Company

FIGURE 1. Data on Lantern Slide Projection.

in teaching medical subjects. It is claimed that they are too expensive, but if the medical student gets more instruction through the judicious use of motion pictures than from stills, the expense involved is immaterial. If a lecture is not worth the outlay of a sum of money to make it of greater value to the student, it is evidently of no great importance.

At the Children's Hospital a number of aids to better visual education have been developed. Some years ago a screen grid was superimposed on certain orthopedic photographs.^{3, 4} With the aid of this grid it is possible to see the deviation from normal of a spine, the tilt of the head in torticollis, the bowing of the legs, asymmetry of the face and so forth. In short, the grid shows up any deviation from the normal. It has had wide use since it was first constructed. Also introduced is so-called "phantom photography," which is a controlled method of double exposure to show the range of mobility in a part.⁵ This is also used effectively by the Orthopedic Department.

About two years ago it seemed that from the orthopedist's point of view the only external part

employment of operative pictures could be made with profit to both the instructor and the student.

For pathologists, a new method of illumination of gross pathologic specimens was instituted a few years ago.⁷ This method shows the surface texture of fresh specimens, whereas the older methods produced what might be called a "photographic map." Color photography of fresh specimens is often far superior to black-and-white photographs of the same specimen.

Infrared photography can sometimes be used to advantage. It must be remembered that infrared light picks up anything blue, such as veins, and makes it plainly visible if it lies near the skin surface, whereas anything red, such as a skin rash, is completely absorbed and does not register.

It is recommended that all persons in charge of lecture halls, auditoriums, and so forth make a check of projection conditions. To be fair to the lecturers using the facilities of any meeting place, the correct focal-length projection lens for the distance from the projector to the screen should be employed. The largest possible screen should be used, bearing in mind that considerable tabulated

s an erosion. If ulceration occurs, it usually affects only the central portion of the erosion and spares the margin.

Ulceration in cutaneous chancres is, according to Fournier,¹¹ in the vast majority of cases due to necrosis and not to secondary infection. This is the reason why even large ulcerated chancres usually heal with a smooth, superficial scar. The absence of significant bacteriologic findings and the inconspicuous scarring in the case reported here permits the conclusion that the ulceration of the chancres was due to necrosis.

Multiplicity of chancres so far as genital chancres are concerned is not unusual. Most authors have given the incidence as approximately 20 per cent. but some have arrived at considerably higher figures, as, for instance, Driver¹² and Blum,¹³ who encountered multiple genital chancres in 38 and 60 per cent of cases, respectively. In extragenital chancres multiplicity is less frequent and probably does not occur in more than 2 per cent of cases. For example, Bulkley¹⁴ observed 1 case of multiple chancres in 116 cases of extragenital chancres, Krefling,¹⁵ 8 in 280, Montgomery,¹⁶ none in 58, Cole,¹⁷ 1 in 61. Tobias,¹⁸ 3 in 65, Downing,¹⁹ none in 38, and Wile and Holman,²⁰ 1 in 68. In most of the reported cases of multiple extragenital chancres the lesions occurred not on the skin but either in the oral cavity or on modified skin like that of the lips and nipples. Thus, multiple chancres of the extragenital skin can be regarded as uncommon. Still rarer is the presence of chancres at far-distant locations of the skin, as in this case. Queyrat²¹ has applied the name "*chancres multipolaires*" to such cases.

SUMMARY

A case presenting three extragenital cutaneous chancres is reported. The chancres were atypical

in appearance because of their large size and the presence of deep ulceration.

Many extragenital cutaneous chancres have an atypical appearance. Primary syphilis should therefore be considered as diagnosis for all cutaneous ulcers or lesions presenting the diagnostic triad of induration, slow course and satellite adenopathy, particularly if there is a profuse serous secretion and the margin of the ulcer is eroded.

270 Commonwealth Avenue

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Two days later, scattered brownish-red papules were first noted on the palms and soles.

Ten days after admission, intensive arsenotherapy was begun. For 10 weeks the patient received each week three injections of 0.065 gm. of Mapharsen and one injection of 0.13 gm. of bismuth subsalicylate in oil. The ulcers showed definite evidence of healing 1 week after the first injection of Mapharsen. After 4 weeks of arsenotherapy, two of the lesions — namely, those on the left side of the chin and in

ed as representing a chancre until proved otherwise by repeated darkfield examination of the lesion, as well as of the satellite lymph nodes, and repeated serologic tests.

In addition to lesions that clinically are on slightly suggestive of chancre but harbor *Tre pallidum*, there are lesions that strongly suggest chancre but are nonsyphilitic. Such lesions have been described under the name "pyoderma chancre formis," first by Sánchez Covisa and Bejarano^{3,4} and later by Gougerot,⁵ Hoffmann,⁶ Krantz,⁷ Stryker and others. They occur in the genital region, on the extragenital skin and the oral mucosa. It is thus an exaggeration to state that it is impossible to make a definite diagnosis of primary syphilis from the appearance of a lesion alone. In Stokes's words,⁹ "the diagnosis of the primary lesion is a laboratory, not a physical or morphologic, problem."

Only with this restriction in mind is it advisable to approach a clinical discussion of the chancre. The diagnostic triad mentioned by Stokes for extragenital, cutaneous chancres one might add for ulcerated chancres the following two signs: a profuse purely serous secretion and an eroded border that is usually slightly raised and shows evidence of infiltration. All five signs were present in the lesion

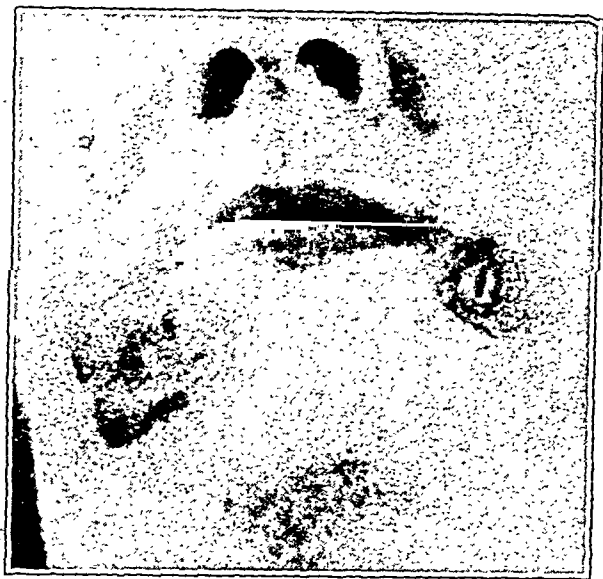


FIGURE 1. Appearance of the Two Chancres Located on the Chin.

the inguinal region — had healed. After 7 weeks, the lesion on the right side of the chin had also healed. Surprisingly little scarring remained, and this was limited to the formerly ulcerated areas. There the skin was smooth, atrophic, depigmented and slightly depressed beneath the level of the surrounding skin. On September 16, 8 weeks after the inauguration of arsenotherapy, Hinton and Wassermann reactions were negative for the first time. They have since remained so. An examination of the spinal fluid on July 27, 1943, was negative.

COMMENT

Chancres frequently do not have the appearance of the typical Hunterian chancre. Milian¹ estimates that only 45 to 50 per cent of all chancres are typical in appearance. He names as atypical forms the giant, dwarf, ulcerated, diphtheroid, crusted and hypertrophic chancre.

Extragenital cutaneous chancres often present an unusual appearance. They are as a rule larger and more inflammatory than the genital variety and are often ulcerated and covered by a heavy crust. The inflammation and induration may suggest a furuncle or carbuncle, the crust of an impetigo (ecthyma) or the ulceration of either carcinoma, tuberculosis or tularemia. Stokes² has therefore stressed the necessity of a "high index of suspicion" when dealing with ulcers or lesions of the skin that present the diagnostic triad of induration, slow course and satellite adenopathy. Lesions presenting these signs should be regarded

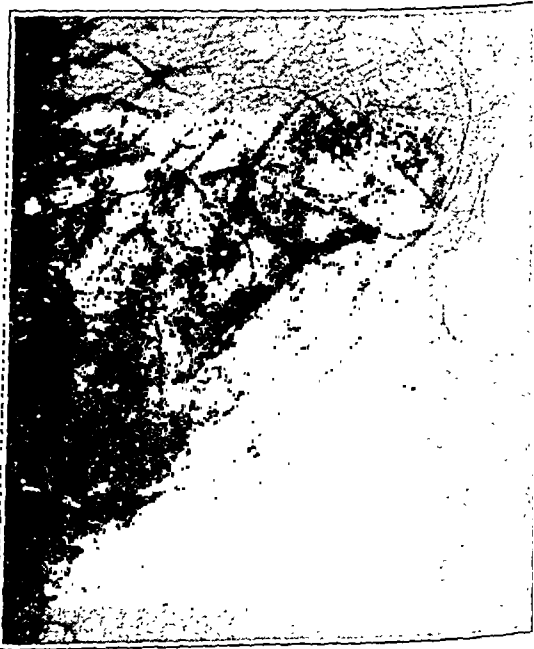


FIGURE 2. Appearance of the Chancre Located in the Left Inguinal Region.

of this patient. The presence of an eroded border is believed to be a sign of great diagnostic value. Dreyer¹⁰ has stated that no sign is of such clearness and constancy and so exclusively limited to syphilitic ulcers as is an eroded margin. Its presence is due to the fact that every chancre manifests itself first

Ichs and Peters⁴ emphasize the importance in treatment of meningococcal meningitis of follow-changes in the cerebrospinal fluid by occasional spinal punctures. They treated 39 cases of meningitis and 7 cases of chronic septicemia at Fort Benning, Georgia, with sulfadiazine or sulfadiazine and serotherapy. There were 2 deaths among the patients with meningitis.

Meyer⁵ treated 33 cases of meningococcal meningitis at the station hospital at Camp Grant between January 4 and July 3, 1943, with sulfadiazine, sulfadiazole and polyvalent serum; there were no fatalities. One patient with the clinical picture of the Waterhouse-Friderichsen syndrome recovered.

Smith, Thomas, Dingle and Finland⁶ review 51 cases of meningococcal infection among patients admitted to the Boston City Hospital in the two-year period beginning September 1, 1940. There were 43 patients with meningitis and 8 with septicemia without it. There were 9 deaths among the first group and none in the latter. Group II meningococcus, these authors state, should be carefully distinguished from the gonococcus, especially when the organism is recovered only from the blood. They emphasize the importance of intravenous administration of the initial dose of sulfonamide drug, the judicious use of spinal punctures for the relief of symptoms of increased intracranial pressure and the frequency of pulmonary involvement by the meningococcus.

The use of sulfamerazine in the treatment of meningococcal infections is reported by Lepper, Sweet and Dowling,⁷ by Geffer, Rose, Domm and Flippin⁸ and by Anderson, Oliver and Keefer.⁹ Lepper and his associates gave sulfadiazine to 96 patients and sulfamerazine to 22 patients with meningococcal meningitis. The mortality rate in each group was exactly the same, and the duration of the illness and incidence of complications in relation to the virulence of the infection were also the same. Sulfamerazine seems to be as effective as sulfadiazine. In their hands the former drug was slightly more toxic. Geffer and his associates treated 45 cases of meningococcal meningitis with sulfamerazine. The mortality rate was 7 per cent, which is compared with a 58 per cent mortality in 40 cases of this disease at the Philadelphia General Hospital in 1935-1937, and 40 per cent in 50 cases reported in 1942. The results also compare favorably with the mortality rate of 13 per cent in the patients who were treated with sulfadiazine. Toxic reactions to sulfamerazine were noted in 11 per cent of the treated patients. Anderson, Oliver and Keefer found that sulfamerazine was clinically effective in total doses that were on the average half to one third smaller than the amount of sulfadiazine usually administered. Toxic reactions were in general of the same character and occurred with about the same frequency as did those caused by sulfadiazine.

The prophylactic use of sulfadiazine during an outbreak of meningococcal meningitis is reported by Lewis, Bolker and Klein¹⁰ and by Kuhns, Nelson, Feldman and Kuhn.¹¹ Lewis and his associates cultured the nasopharynx of contacts of patients with meningococcal meningitis. The carrier rate averaged 13 per cent but in some groups was as high as 42 per cent. The carriers were admitted to a special ward and given 2 gm. of sulfadiazine daily for two days and 1 gm. daily for two days. Fluids were forced. No ill effects were noted in 897 carriers. Every person who showed a positive nasopharyngeal culture subsequent to treatment with sulfadiazine was given a course of sulfanilamide. This was necessary in 30 carriers, in all of whom but 1 the culture became negative. The authors state that the use of small doses obviates the risks of toxic reactions to the drug and the need of extensive laboratory facilities. Kuhns and his associates administered 2 gm. of sulfadiazine a day for two days to 15,000 soldiers in residence at two posts where meningococcal meningitis was particularly prevalent during the spring of 1943. Only 2 cases of the disease were reported in the treated cases during a subsequent period of eight weeks' observation, as compared with 40 cases among 18,800 controls. No serious toxic reactions were noted and the treated men continued their usual daily activities.

Fulminating meningococcal septicemia with extensive purpuric hemorrhages into the skin and the adrenal gland has been the subject of numerous reports. Thomas³ found this combination of symptoms, known as the Waterhouse-Friderichsen syndrome, in 17 of 23 patients who died of septicemia and in 1 additional patient there was edema and congestion of the adrenal glands. Blood transfusion, plasma infusion and adrenocortical extract are recommended by Thomas for the treatment of shock in these patients. In a few cases he obtained good results with epinephrine administered by the constant-drip method. Desoxycorticosterone was used but without clear-cut evidence of benefit. Banks and McCartney¹² submit evidence that the meningococcal adrenal syndrome is a composite entity. It can be differentiated into a pure adrenal syndrome and a mixed or encephalitic one. The former is not necessarily fatal. Eleven cases are reported, 8 of which were fatal. Evidently, prompt diagnosis and immediate treatment of the infection with sulfonamide drugs and vigorous replacement therapy for the adrenal crisis may lead to recovery, at least from the pure adrenal syndrome. Gordon and Shimkin¹³ report a case of the Waterhouse-Friderichsen syndrome in which autopsy showed focal necrosis of the pituitary gland, in addition to congestion and microscopic areas of extravasation of red cells into the medulla of the adrenal glands. The authors claim that the changes in the adrenal glands were insufficient to explain the acute adrenal failure, and state that it is possible that the syndrome

MEDICAL PROGRESS

NEUROLOGY*

H. HOUSTON MERRITT, M.D.†

BOSTON

PROGRESS in neurology has been greatly influenced by the war. Publication of results of experimental work in the fundamental sciences has been curtailed because of the shortage of physicians, and because much of the research that is being conducted is along lines of vital importance to the war effort and will not be published until after the war. On the other hand, the increase in the incidence of infectious diseases that always accompanies war has given an opportunity to test newer methods of treatment on large numbers of cases, and the global nature of the conflict has awakened new interest in tropical and other diseases that are seldom seen in this country in normal times. In addition, the injuries to the brain and peripheral nerves occurring in war have stimulated investigative work into the mechanism of cerebral concussion and nerve repair. These two topics are omitted from this article since they will be discussed in the review of advances in neurosurgery.

INFECTIOUS DISEASES

Meningococcal Meningitis

Great strides have been made in recent years in the treatment of meningococcal meningitis. The results obtained with chemotherapy are in striking contrast to those formerly obtained with serotherapy. It is gratifying to note that the use of intraspinal therapy is rapidly being discarded. Uniformly good results in the treatment of meningococcal meningitis by sulfonamide drugs have been reported by various observers. Daniels, Solomon and Jaquette¹ treated 112 patients with meningococcal infections at Fort Bragg, North Carolina, between January 1, 1942, and April 17, 1943. Eighty patients with meningitis and 32 with meningococcemia with no meningitis were treated with sulfadiazine, with only 1 death in the former group and none in the latter. The patients were divided into two groups according to the amount of drug exhibited. The first group received intravenously an initial dose of 0.1 gm. of sodium sulfadiazine per kilogram of body weight, followed by half the initial dose parenterally every eight hours until the patient was able to take the drug by mouth in doses of 1.0 to 2.0 gm. every four hours, so that a blood

concentration of 15 mg. per 100 cc. might be maintained. The second group received intravenously an initial dose of 0.05 gm. per kilogram of body weight, followed in four hours by a dose of 0.05 gm. per kilogram. The dose was repeated every eight hours until the patient was able to take the medicine by mouth. The results in both groups were excellent, but the patients who were treated with the smaller doses required a smaller total dosage of the drug than did the others. The duration of fever and length of stay in the hospital were also less in this group, and renal complications were absent, in contrast to the occurrence of hematuria in 15 per cent and anuria in 7 per cent of the group that received the larger dosage.

Hill and Lever² treated 68 cases of meningococcal infections with sulfadiazine at Camp Edwards, Massachusetts, between January 1 and April 15, 1943, with no fatalities. They stress the importance of early diagnosis and treatment. Treatment can be instituted without waiting for bacteriologic diagnosis when the four combined symptoms, headache, vomiting, chill and rash, are present. These authors emphasize the necessity of administering the initial doses intravenously and the maintenance of an adequate fluid intake. Thirteen of their patients had meningococcemia with no meningitis. Positive blood cultures were obtained in 40 cases. The spinal fluid was clear in 31 of the 62 cases in which a spinal puncture was done. Organisms were frequently recovered from clear fluids.

Thomas³ reports an outbreak of meningococcal meningitis and septicemia in the Fourth Service Command between December, 1942, and June, 1943, during which there were 1935 cases. The mortality rate was 3.3 per cent, which is in striking contrast to the 39 per cent mortality reported by Simmons and Michie for the 6000 cases that occurred in the United States Army during World War I. Two thirds of the cases reported by Thomas developed among new troops, and 80 per cent of the 55 fatal cases occurred in this group. Eighteen of the 46 autopsied cases showed hemorrhages into the adrenal glands. This is regarded as an index to the severity of the septicemia and presents an additional feature for therapeutic consideration. Thomas states that early diagnosis and prompt skillful treatment based primarily on administration of suitable sulfonamide compounds will still be important even if prophylactic chemotherapy prove highly effective.

*From the Department of Neurology, Harvard Medical School, and the Neurological Unit, Boston City Hospital.

†Associate professor of neurology, Harvard Medical School; assistant director, Neurological Unit, Boston City Hospital.

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resulted from damage to the pituitary gland alone or in combination with the minimal adrenal changes and the effects of the septicemia. Herbut and Manges¹⁴ review the history of the Waterhouse-Friderichsen syndrome and report 4 cases. They conclude that there is no proof that death in these cases is due to adrenal failure rather than to toxicity caused by invasion of the blood stream. Williams¹⁵ reports 17 fatalities resulting from acute fulminating meningococcemia. Adrenal hemorrhages were found at autopsy in only 9 of these cases. He concludes that the adrenal hemorrhage is but an incident in an explosive disease process that overwhelms all bodily resistance.

Bernstein¹⁶ reports a case with causalgia of the right arm and purpuric dry gangrene of the toes and scattered areas of the skin as an example of a rare complication of meningococcal meningitis.

Penicillin Therapy in Bacterial Meningitides

There have as yet been few reports in the literature regarding the value of penicillin in the treatment of infections of the nervous system, and its place in the treatment of meningitis, brain abscess and so forth has not been established.

Pilcher and Meacham^{17, 18} report on the use of penicillin in the treatment of meningitis produced experimentally in animals by the intraspinal inoculation of staphylococci and pneumococci. They found that intravenous use of penicillin had no beneficial effect on staphylococcal meningitis. Intrathecal injections, even in small amounts, lowered the mortality rate from 93 to 54 per cent. They resulted in a pleocytosis in the cerebrospinal fluid but no other toxic effects were noted. Similar good results were obtained in the treatment of pneumococcal meningitis. Both intrathecal and intravenous administration of penicillin was necessary in pneumococcal infections, since many of the animals treated only by the intrathecal route died of pneumococcal pneumonia.

Rammelkamp and Keefer¹⁹ studied the concentration of penicillin in the cerebrospinal fluid after intravenous and intrathecal administration in normal subjects and in patients with meningitis. Penicillin did not pass through the blood-brain barrier in significant quantities when injected intravenously. After the intrathecal injection of 5000-10,000 Florey units, penicillin was slowly absorbed and slowly excreted in the urine. It was detected in the cerebrospinal fluid thirty-one hours after injection of 10,000 units. Absorption from the subarachnoid space was more rapid in the patients with meningitis. It was found at autopsy in the fluid from both the cisterna magna and third ventricle of 2 patients who had received the agent intraspinaly several hours before death. In normal subjects the intraspinal injection of 10,000 units caused headache, vomiting, increased intracranial pressure and pleocytosis in the cerebrospinal fluid similar to that seen

after the intraspinal injection of serum, lipiodol or air. The intraspinal injection of 5000 units in normal subjects produced only slight headache and slight pleocytosis in the cerebrospinal fluid. The intrathecal injection of 3000 to 10,000 units in patients with meningitis produced no untoward symptoms. Since penicillin is known to be extremely effective as an antibacterial agent against the streptococcus, pneumococcus and staphylococcus and since meningitis and brain abscess caused by the latter two are resistant to sulfonamide therapy, Rammelkamp and Keefer suggest that the intrathecal injection of penicillin may be a useful method of treating these conditions. Since an effective concentration of the active substance can be maintained for about twenty-four hours without undue toxic reactions, the initial dose should not exceed 10,000 units and subsequent injections of 5000 units may be given every twenty to twenty-four hours. If bacteremia is present, penicillin should be given intravenously as well as intraspinaly.

Evans²⁰ used penicillin in the treatment of 1 patient with pneumococcal meningitis and 2 patients with staphylococcal meningitis, with recovery in all 3 cases. In the first case, pneumococcal meningitis developed following fracture of the skull. In the second case, infection of the meninges by the staphylococcus was secondary to sinusitis and intracerebral abscess. The third patient developed staphylococcal meningitis subsequent to an operation for the removal of a cord tumor in the cervical region. Large doses of penicillin were administered intravenously, intramuscularly and intrathecally in all 3 cases. Sulfadiazine was also used in the treatment of the first patient, but Evans gives the major credit for the cure to penicillin and thinks that its intrathecal administration of penicillin in such cases is of great value.

Cerebral Malaria

Infection with malaria organisms is one of the major problems of military medicine, and as a result the literature of the past year contains numerous articles on various aspects of the infections, including the symptoms and signs of cerebral involvement.

Simpson and Sagebiel²¹ report 12 cases of cerebral malaria that were treated at a United States naval base hospital without a fatality. The dominant symptom was sudden onset of convulsions and coma. An acute confusional psychosis developed in 6 cases. The febrile reactions were highly irregular, with no tendency to follow a forty-eight-hour cycle. The cerebrospinal fluid was examined in 8 cases. It was under increased pressure, and pleocytosis was present in those cases manifesting marked meningeal symptoms. They state that prognosis depends on early diagnosis and prompt treatment. Quinine dihydrochloride, 7½ gr. in 250 cc. of normal saline solution, was administered

ravenously every eight hours until the patients are able to take quinine by mouth. Sedation and absolute bed rest are considered of importance in the therapy.

Galbot²² calls attention to the fact that malaria may stimulate disease of every part of the body, and that the absence of chills and fever should not rule out its occurrence in people who are living in other areas of endemic malaria. He divides the typical cases into twelve groups, four of which are of special interest to the neuropsychiatrist. In one group there are various manifestations of cerebral malaria, with headache, fever and prostration, including medical shock, heat exhaustion, acute delirium, acute mania or an afebrile psychosis. The symptoms clear up or greatly improve on antimalarial therapy. In the second group there is complaint of visual disorder, with headache, often of long duration. Some of the patients have typical optic neuritis, with clouding or dimness of vision, temporal or frontal headache and deep pain in the orbit, which is made worse by ocular pressure. Under antimalarial therapy these patients improve, some with varying degrees of residual visual impairment. Patients in the third group have signs and symptoms of other cranial-nerve involvement, frequently that of the eighth nerve, with resulting vertigo and deafness. A pure malarial basilar meningitis is sometimes seen. The fourth group comprises patients with vague complaints of neuralgia, fatigue or other inconsequential symptoms often labeled as psychoneurotic. The diagnosis of malaria is established by the findings of positive blood smears, and the symptoms are relieved by quinine therapy.

Most and Meleney²³ stress the importance of early diagnosis and adequate treatment of infections with *Plasmodium falciparum*. Unless one is familiar with the extremely varied clinical picture that infection from the organism may assume and the possibility of the development of alarming symptoms requiring early and intensive therapy, the infection may remain unrecognized and may even terminate fatally. Stupor and coma are the most frequent evidences of involvement of the nervous system. In some cases convulsions, stiffness of the neck, hyper-reflexia and the Babinski sign are present. Occasionally there is intermittent rigidity or sucking and grasping reflexes. Incontinence of the sphincters is frequent. On the whole, the clinical picture is similar to that seen in acute meningitis or encephalitis. Mental symptoms are occasionally the outstanding feature at the onset and may result in the admission of the patient to a psychiatric institution. Confusion, restlessness and negativism are usual findings. Such patients must be watched closely, since they may become manic or commit suicide. Quinine dihydrochloride, 6 gm., should be given intravenously every four

hours to patients in coma or with predominant cerebral signs. Spinal drainage may be of value in restoring consciousness. Fluids by vein should be administered freely, and nicotinic acid in doses of 100 mg. should be added to the infusion along with each dose of the quinine dihydrochloride in order to secure maximal dilatation of the cerebral capillaries.

The pathology of cerebral malaria is described by Dhayagude and Purandare.²⁴ In the course of fifteen years they found malarial parasites in the capillaries of the brain in 55 of 97 cases of malaria. Fever and coma were present in 28. Other symptoms included paresis of the limbs, aphasia, dysentery, pneumonia, rigidity of the neck and exaggerated reflexes. The brain appeared grossly normal in 12 of the 55 cases, and in the remaining 43 there was a slate-gray discoloration of the brain substance. On microscopic examination the capillaries of all 55 patients were filled with malarial parasites and their pigment. Punctiform hemorrhages were found in the subcortical region in 2 cases. Malarial granuloma was present in 10 cases. Older granulomas consist of a central capillary surrounded by a mass of neuroglial cells. *P. falciparum* was the infecting type of parasite in the cases with granuloma. The granulomatous lesions, according to these authors, provide the pathological basis for mental disturbances designated as "malarial psychosis."

Subdural Empyema

Kubik and Adams²⁵ present a study of 14 patients with subdural empyema. Their article is the most complete analysis of the clinical features and pathological observations yet recorded in the literature. The sources of infection were paranasal sinusitis in 12 cases, otitis media in 1 case and bronchiectasis with metastatic infection in 1 case. The symptoms in the cases complicating sinusitis were fairly uniform and consisted of exacerbation of chronic sinusitis, orbital swelling, headache, at first localized and later becoming generalized, fever, stiffness of the neck, drowsiness or stupor and focal neurologic signs. Hemiplegia or hemiparesis was present in nearly all cases, and Jacksonian seizures often occurred. The cerebrospinal fluid was under increased pressure, with an increase in cell count and protein content. The sugar content was normal, and the fluids were sterile. The course was rapidly progressive, death in 12 cases occurring within six to twenty days after the onset of the headaches. Two patients recovered after surgical drainage of the empyema. Infection of the subdural space occurred by direct extension through the dura or as a result of thrombophlebitis of the venous sinuses. The subdural pus covered the greater part of the lateral surfaces of the frontal lobe, and in the corresponding area there was a localized subarachnoid exudate but scarcely any generalized leptomeningitis.

gitis. In the underlying cortical gray matter there was severe ischemic necrosis and in most cases thrombosis or thrombophlebitis of the subarachnoid veins. Surgical treatment should consist of drainage through a craniotomy and not through the frontal sinus or a mastoidectomy wound.

Mumps

McGuinness and Gall²⁶ analyze the data on 1378 cases of mumps at Camp McCoy, Wisconsin. Neurologic complications were present in 55 cases (4 per cent). Headache, nausea, drowsiness and stiff neck were the symptoms and signs indicative of involvement of the nervous system in all but 3 of these 55 patients. In these 3 the syndrome was that of a primary subarachnoid hemorrhage in one patient, that of an intracerebral hemorrhage in the second and that of an acute polyneuritis with facial diplegia in the third. The cerebrospinal fluid was bloody in the first two cases, and in the third the fluid contained 16 white cells per cubic millimeter and 135 mg. of protein per 100 cc. The first patient had a mild parotitis, and in the third patient the signs of involvement of the nervous system developed twenty days after the onset of parotitis. In the second case there was no parotitis and the diagnosis of mumps was based on a complement-fixation test. The authors attribute the neurologic involvement in all 3 cases to the mumps infection but it seems more likely that they were only coincidental complications.

Herpes Zoster

Denny-Brown, Adams and Fitzgerald²⁷ report on the pathologic features of 3 cases of herpes zoster. In 2 patients the herpetic eruption was in the thoracic region and the corresponding dorsal root ganglion was the site of an inflammatory necrosis. In addition, there were degeneration of the related motor and sensory roots, severe neuritis, unilateral segmental poliomyelitis and localized leptomeningitis. The third case, with eruption in the occipital and auricular regions and a transient facial (Ramsay-Hunt syndrome) and lingual palsy, was of special interest because of the rarity of autopsy examination in such cases. The authors found necrotizing ganglionitis of the second cervical ganglion, unilateral segmental poliomyelitis in the cervical cord, motor neuritis of the facial nerve and mild inflammatory reaction in the medulla. There was no destruction of the cells in the geniculate ganglion, but some lymphocytic infiltration was present in the fibers of the facial nerve adjacent to the ganglion.

Taterka and O'Sullivan²⁸ report 2 cases of herpes zoster with paralysis and atrophy of muscles of the extremities and summarize the data on 42 previously reported cases. The muscular involvement does not necessarily coincide with the herpetic eruption in localization and extension. The time interval

between the vesicular eruption and appearance of paralysis may range from one day to two months.

Poliomyelitis

The concepts of muscular dysfunction in acute poliomyelitis advanced by Sister Kenny were subjected to analysis by Watkins, Brazier and S.C. and Moldaver.³⁰ Watkins and his associates, who used the electromyograph, state that of the concepts of Kenny the only one upheld by objective measurement is that of inco-ordination and this term is misleading. They demonstrated not only simultaneous activation of protagonist and antagonists but also intermittent synchrony of motor discharges from opposing muscles such as is found in peripheral-nerve injuries during regeneration of axones. "Disordered reciprocal innervation" seems to be a more descriptive term for this type of dysfunction. Moldaver³⁰ explored neuromuscular degeneration in poliomyelitis by the chronaximetry method; the so-called "spasm" was studied in some patients, mostly by electromyograms. He concluded that "spasm" does not lead to neuromuscular degeneration. In paralytic and paretic muscles called "alienated," there is always some degree of neuromuscular degeneration. Among these muscles some are partially denervated; these have a good chance to recover. Others are totally denervated and cannot therefore recover. There is no clinical evidence of so-called "inco-ordination" in the ordinary sense. The patient attempts voluntarily or involuntarily to use a stronger muscle for a weak or paralyzed one. This abnormal use of an extremity is substitution and not inco-ordination.

Rickettsial Diseases

Dyer³¹ reviews the rickettsial diseases and points out the constancy of cerebral symptoms in epidemic and endemic typhus fever. Nervous and mental symptoms are also frequent. In Rocky Mountain spotted fever there are restlessness, insomnia, disorientation and, in severe cases, delirium. In fatal cases coma usually precedes death.

EPILEPSY

Diagnosis

In civil life the diagnosis of epilepsy can be established by observation of the patient over a period of months or years. In military hospitals it is important for various reasons to establish the diagnosis as soon as possible. In patients with infrequent seizures, the main diagnostic aids are electroencephalography and the observation of seizures artificially produced by hydration or overventilation.

Garland, Dick and Whitty³² used the water-Pitressin test in 96 patients, including 20 controls. The patients were kept in bed throughout the test and for twenty-four hours afterward. Five hundred

centimeters of water was given hourly from 8 a.m. until the test was discontinued, the usual amount being 5500 cc. Pitressin was given hourly from 8 a.m. onward, the doses being 0.2, 0.3, 0.4 and 0.5 cc., followed by four doses of 0.5 cc. each. Blood-pressure readings were made at frequent intervals, and the patient was weighed every three days. Fluid intake and output, including vomitus, were also measured to determine the amount of fluid retention. If a fit occurred, the test was stopped at once and 1 gr. of phenobarbital was given by mouth. It was also stopped if there was severe distressing vomiting, abdominal discomfort or severe and persistent headache. Fits usually occurred from 5 p.m. onward. No serious untoward effects were noted. Convulsions resulted in 17 (39 per cent) of the 44 patients with epilepsy, 12 (38 per cent) of the 32 patients with doubtful epilepsy and in none of the 20 control patients with hysterical convulsions.

Swab³³ found the electroencephalogram to be of great value in the diagnosis of epilepsy in a Navy hospital.

Robinson³⁴ tested the value of hyperventilation in the electroencephalogram in the diagnosis of epilepsy. One hundred and forty-six patients were subjected to a six-minute period of hyperventilation. Seizures occurred in 14 (10 per cent). The seizures were of the petit-mal type in 12 patients and of the grand-mal type in 1, and took the form of involuntary crying in 1. The seizures that resulted from hyperventilation were similar to the patient's spontaneous seizures. The petit-mal seizures occurred during hyperventilation. The single grand-mal seizure followed the period of overbreathing by 1 and a half minutes. Of the 14 patients who had a seizure related to hyperventilation, the resting electroencephalogram was abnormal in 12 (85 per cent). The electroencephalogram showed slow waves during hyperventilation in all 14 cases. Robinson concludes that the value of overbreathing in the diagnosis of epilepsy lies in its simplicity of application and the specificity of response that is obtained. It enables the physician to observe the usual seizure pattern. The disadvantages are that seizures result in only a small percentage of cases and that the method requires the active co-operation of the patient. The test does not exclude bizarre hysterical episodes. By contrast the electroencephalogram has the advantages of permanency of record, the need of a minimum degree of co-operation on the part of the subject, the possibility of localizing the focus of a circumscribed lesion and of forms that are often specifically diagnostic in themselves. The disadvantage is the nonspecificity of the abnormal potentials occurring in some of the activities of epileptics, in some persons with mental deficiency, psychosis or behavior disorders and in cases of increased intracranial pressure.

Merritt and Brenner³⁵ report on 3 patients with convulsive seizures who had normal air encephalograms, seven, twenty and thirty months, respectively, after their first convulsions but were subsequently proved to have brain tumors. Cerebral tumors, they say, are not apt to produce any change in the ventricular system unless they are large enough to produce focal neurologic signs or increased intracranial pressure. If in the absence of these it is decided that an air study is advisable, a negative report should not be accepted as conclusive proof that no tumor is present.

Treatment

Cohen, Coombs, Cobb and Talbott³⁶ found that azosulfamide exhibited anticonvulsive action in patients with epilepsy. Associated with the anticonvulsive effects were a decrease in the carbon dioxide power of the serum and an elevation in serum chlorides. In comparing the changes in the serum produced by azosulfamide with those accompanying the administration of phenobarbital they found that a positive potassium balance coincided with the anticonvulsive effect of both drugs. Ammonium chloride produces the same degree of acidosis as does azosulfamide, without alteration of potassium exchange, but the former has no anticonvulsive effect. Phenobarbital produces no acidosis but a positive potassium balance and has an anticonvulsive effect, which suggests that the acidosis is not necessarily the crucial factor in anticonvulsant action.

Davidoff and Doolittle³⁷ used sodium 5-ethyl, 5-(methyl, 1-butenyl) barbiturate (Delvinal Sodium Vinobarbital) in the treatment of patients with convulsive seizures. They found that it was more effective than phenobarbital in the control of petit-mal seizures and did not produce the degree of drowsiness that follows the administration of the latter. Because of its effect on psychomotor activity it is a valuable adjunct to other anticonvulsant drugs, such as Dilantin Sodium, in the treatment of grand-mal or severe motor seizures. Because of its rapid action and relatively low toxicity, the oral administration of the drug is of distinct value in the treatment of serial seizures and their sequelae.

Price, Waelsch and Putnam³⁸ report that *dl*-glutamic acid hydrochloride is beneficial in the treatment of petit-mal and psychomotor seizures. Petit-mal seizures were decreased in frequency, and there was subjective and objective improvement in the mental and physical alertness of the patients. Grand-mal seizures were not affected by administration of the drug.

INTRACRANIAL ANEURYSMS

Intracranial aneurysms continue to receive considerable attention. Sahs and Keil³⁹ review the clinical features in 64 cases in which the diagnosis

of subarachnoid hemorrhage caused by ruptured intracranial aneurysm was made. The presence of aneurysm was verified at autopsy in 12 cases. Eighteen of the 64 patients died in the hospital, 22 were discharged well, and 24 were improved but were left with sequelae such as hemiplegia, ocular palsy, aphasia and disturbance of the visual fields.

From a study of 10 cases, Globus and Globus⁴⁰ conclude that rupture of an intracranial aneurysm into the substance of the brain and into the ventricles is preceded by softening of brain surrounding the vessel. Changes in the brain tissue parallel the progressive pathologic alterations in the aneurysmal wall that culminate in its rupture. The escaping blood breaks through a residual zone of partially softened brain tissue separating the so-called "hemorrhagic cavity" from the adjoining compartment of ventricular cavities, and floods the latter as the fatal termination. A fatal issue occurred as the result of intracerebral and intraventricular hemorrhage in 10 of the 20 verified cases of intracranial aneurysm.

POLYCYTHEMIA VERA

Tinney, Hall and Giffin⁴¹ report neurologic symptoms in 78 per cent of 163 cases of polycythemia vera. Fifty-five patients sought treatment primarily because of neurologic complaints. Subjective complaints, such as weakness, fatigue, insomnia, drowsiness, irritability and loss of memory, were so frequent, nonspecific and varied that patients exhibiting them were thought to have a functional disorder. Objective neurologic signs occurred in 17 per cent of the series and resulted from thrombosis of a cerebral vessel or from cerebral hemorrhage.

PERIODIC PARALYSIS

Brown, Currens and Marchand⁴² describe a hitherto unrecognized syndrome associated with potassium loss in patients with chronic nephritis. The syndrome is characterized by episodes of flaccid paralysis of the extremities resembling that seen in familial periodic paralysis, low T waves in the electrocardiogram similar to those seen in patients with potassium depletion, and signs of chronic nephritis. The authors conclude that the muscular weakness and the electrocardiographic changes are related to the low level of potassium in the serum, which results from the excessive excretion of potassium by the diseased kidneys.

818 Harrison Avenue

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SE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30321

PRESENTATION OF CASE

First admission. A forty-four-year-old musician entered the hospital because of weakness and tarry stools.

The patient had been in apparent good health until thirteen years before admission, when he developed epigastric pain coming on a few minutes to two hours after meals. It was not severe, was aggravated by excitement and was relieved by soda at first and Amphogel later. It radiated through to the back. The attacks would last for a few weeks and then disappear for months. Eight years before entry he had an episode of feeling faint and noticed profuse perspiration, followed by the passage of a dark molasses-like stool. He fainted and was taken to a hospital in another city. He was given several blood transfusions and was discharged. Since that time he had had recurrent attacks of similar character, for which he was admitted to a community hospital one or ten times. Repeated and extensive studies at that hospital were negative except for blood in the stools and a mild hypochromic anemia, for which he was repeatedly transfused. A gastroscopy was said to show a gastric polyp and possibly a benign peptic ulcer.

Since the first episode the patient had more or less limited himself to a bland diet and had taken six meals daily. Although he led a rather strenuous and perhaps irregular life, he did not drink alcoholic beverages or smoke. Asparagus, turnips and cabbage gave him hives. Fried foods brought about epigastric pain. No statement was made about the relation of the pain and the bleeding. He had had no jaundice or clay-colored stools. He had had no sore tongue, difficulty in swallowing or genitourinary or cardiorespiratory symptoms.

The patient had lived in the Philippines until he was nineteen years old. He had had smallpox as a child but had had no other known illnesses.

Physical examination showed a well-developed, well-nourished pale man in no distress. The heart and lungs were normal. There was moderate mid-epigastric tenderness to deep palpation, but no masses or spasm.

*On leave of absence.

The blood pressure was 120 systolic, 80 diastolic. The pulse was 82, the temperature 99°F., and the respirations 20.

Examination of the blood showed a red-cell count of 5,300,000, with 12 gm. of hemoglobin, and a white-cell count of 7600, with 75 per cent polymorphonuclears, 20 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils. The platelets were normal. A blood Hinton test was negative. The urine was normal. Two guaiac tests on stools were negative. The blood serum nonprotein nitrogen was 24 mg. per 100 cc., and the protein 9 gm. The prothrombin time was normal, and the clotting time 7 minutes. The hematocrit was 46.8 per cent. The corrected sedimentation rate was 1.7 mm. per minute. A second hematocrit was 42 per cent. A bromsulphalein test gave 5 per cent retention. A tuberculin test with a 1:50,000 dilution was negative.

A gastrointestinal series showed a normal esophagus. The stomach contained a small amount of fluid. No definite polyp or ulcer crater could be demonstrated. The duodenal cap was quite tender and on a spot film showed an area suggestive of a small crater on the posterior wall. Fluoroscopic examination of the chest showed areas of increased density in the right upper lobe and shadows that were suggestive of small cavities.

Following the x-ray films of the chest two gastric aspirations were examined for acid-fast bacilli, without success. Sputum examinations were also negative. For a while the patient was put under respiratory precautions. At the end of the second hospital week a gastroscopy revealed a network of what appeared to be dilated veins 1 to 3 mm. in diameter covered with a rather smooth slightly reddened mucosa; they were situated on the anterior wall, extending from the angulus to the cardia. Examination was otherwise negative. A repeat gastrointestinal series showed no additional findings. The patient was discharged against advice on the fifteenth hospital day.

Second admission (five months later). Following discharge the patient was in excellent health for three weeks, having had no recurrence of epigastric pain or of tarry stools. At that time, following an upper respiratory infection, he passed a black stool and was admitted to a community hospital for ten days. There was no further melena and he was sent to this hospital for further studies.

Physical examination was essentially the same as before.

The blood showed a red-cell count of 3,160,000, with 7 gm. of hemoglobin, and a white-cell count of 4200, with 56 per cent polymorphonuclears, 40 per cent lymphocytes and 4 per cent monocytes. The red cells were hypochromic, with moderate variation in the size of the cells. The urine was normal. One stool examination showed a ++ guaiac test. The nonprotein nitrogen was 28.5 mg. per 100 cc., and the protein 8.4 gm., with 6.1 gm. of albumin

and 2.3 gm. of globulin. The cephalin-flocculation test was \pm in twenty-four hours and $++$ in forty-eight hours. A bromsulfalein test showed 5 per cent retention.

A gastrointestinal series revealed considerable thickening of the mucosal folds in the stomach, without definite ulceration. The distal part of the duodenum remained narrow, and there was slight irregularity in the area previously described that was suggestive of a crater. The remainder of the examination was negative. X-ray films of the chest revealed no change from the previous examination. Gastric aspiration showed no acidity in the original contents or in that twenty-four hours after histamine; there was a $+$ guaiac test.

A gastroscopy showed essentially the same findings as noted before, with the addition of two areas on the anterior wall that measured 4 mm. in diameter and were white. There was no blood in the stomach.

The patient was given several transfusions of whole blood, and on the twenty-first hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. E. STANLEY EMERY, JR.* This protocol presents a forty-four-year-old musician who, for thirteen years, had suffered from epigastric distress, which could have been compatible with a duodenal ulcer. For eight years he had been having frequent attacks of gastrointestinal bleeding. Another possibly important point in the history is that he lived in the Philippines until he was nineteen years of age. He is said to have been allergic to certain foods and had what appears to have been a chronic stationary process in the right upper lobe of his lung. X-ray study revealed a narrowing and slight irregularity of the duodenum that was suggestive of a crater, but I gather that it was not considered characteristic for a duodenal ulcer. Furthermore, gastroscopy revealed a curious network of what appear to be dilated veins on the anterior wall of the stomach. The protocol suggests that bleeding was the major problem. From the data presented we have to decide why this patient continued to bleed.

The leading questions are as follows: Did this patient have an ulcer? Was ulcer alone responsible for the bleeding or was there another condition superimposed or co-existent with an ulcer? Was there some condition that was not only responsible for the bleeding but also simulated an ulcer?

Bockus¹ lists twenty-three causes for gastrointestinal bleeding, and it is obvious that in the time allotted I cannot discuss all these causes. I am therefore going to consider the findings as presented with the hope that I may get a clearer idea of the nature of the symptoms and the laboratory find-

ings and then discuss those things that seem pertinent.

The protocol tells us that the patient had been in good health until the age of thirty-one, when he developed epigastric pain that was not severe. I wish that I knew more about the nature of the symptoms because a differential diagnosis involves the question of ulcer may be settled by an accurate evaluation of the symptoms. It might be helpful to know whether the distress coming on a few minutes after eating was the same or different from that beginning two hours after eating. The exact point to which the distress radiated to the back might also have some diagnostic significance.

Eight years before entry he had the first of a number of severe bleeding attacks for which he was studied nine or ten times at a community hospital. All these studies were apparently negative except for a mild hypochromic anemia and a gastroscopy that was said to have shown a gastric polyp. It is a suggestion of a benign peptic ulcer. It would be helpful to know who did the gastroscopy, since the value of procedures of this kind is in direct proportion to the experience and ability of the man performing them. The polypoid appearance may be of significance and will be discussed further later on.

The patient had followed a somewhat limited diet consisting of six meals daily, but we are not told whether the painful symptoms were ameliorated by the frequent feedings. He did not drink alcohol which eliminates one cause of portal cirrhosis. He was allergic to asparagus, turnips and cabbage in that they gave him hives. Fried foods brought on epigastric pain, but we are not told whether this was the same type of pain of which he usually complained. I should like to know this, although I gather little significance was given to this fact since there is no statement that x-ray films of the gall bladder were taken. I cannot lay much importance to this statement because many patients either with or without organic disease, complain of indigestion from fried foods that has to do with the way they are cooked or something of that sort. It is said that no statement was made about the relation of pain and bleeding. I am not sure why this was put in; furthermore, if there were a positive relation, I should not know how to interpret it. The patient had never had clay-colored stools, which is negative evidence for biliary disease. He had had no sore tongue or difficulty in swallowing; in other words, no evidence was found for a deficiency. There were no genitourinary or cardiorespiratory symptoms. The history therefore does not suggest that the bleeding was secondary to cardiac insufficiency.

Having lived in the Philippines until he was nineteen years of age causes us to think of some parasitic infestation as the cause of the gastrointestinal bleeding. I have seen one patient infested with *Ascaris lumbricoides* who had definite attacks of epigastric

*Senior associate in medicine, Peter Bent Brigham Hospital.

simulating an ulcer that were completely re- after expulsion of the worms. Hookworm infection may cause bleeding, usually of a chronic type. Schistosomiasis is another disease that is a frequent cause of bleeding, but the mechanism is a different one, for which there is no evidence in this case. Furthermore, I assume that the patient was thoroughly studied for parasites in the stools and no evidence of their presence is recorded. There was no eosinophilia and, therefore, I think that this possibility can be ignored.

The protein was 9 gm. per 100 cc., and at a later admission, 8.4 gm. with 6.1 gm. of albumin and 2.3 gm. of globulin. This marked elevation of blood protein is difficult to understand, and in talking with Dr. Howard Armstrong he could make only two suggestions: either it was the result of marked dehydration or the test was done in an extremely dry laboratory. The first hematocrit was 46.8 per cent, and the second 42 per cent, neither of which suggests marked dehydration. There is nothing in the patient's history to suggest dehydration, although the cell count was high for a person who had been recently bleeding. The sedimentation rate was very rapid, which may be evidence for something more than a peptic ulcer. A gastrointestinal series showed a dilated duodenal cap and an area suggestive of a crater on the posterior wall. At the time of the first report no mention was made that the duodenum was narrow, but a second report stated that it remained narrow. I wonder if I may see the x-ray films.

DR. LAURENCE L. ROBBINS: These films were looked out at random, and they demonstrate the process in the right upper lobe. The lesion has the appearance of a rather long-standing tuberculous cavity.

DR. EMERY: One wonders whether these findings could have been due to some fungus infection, which, although rare, can produce lesions in the gastrointestinal tract that are responsible for pain and bleeding. Actinomycosis and blastomycosis have both been reported in the duodenum, but they are extremely rare. A second examination of the findings five months later reported no change, which I suppose argues against a fungus or any active process in the chest, but I should like to get the opinion of the roentgenologist on this point.

DR. ROBBINS: It certainly could be a fungus infection.

DR. EMERY: Would the fact that it had not changed in five months tend to rule it out?

DR. ROBBINS: No; furthermore, tuberculosis may show no change by x-ray over a long period of time. The gastrointestinal examinations were done at various times. We can definitely rule out varices of the esophagus. The area that was questioned several times about the possibility of a crater was this narrow distal portion of the cap, but we could never be positive about it. These are thickened

mucosal folds in the cap and make one suspicious of some inflammatory process in that area. The stomach shows some thickening of the mucosal folds and some increase in the amount of secretion, both of which are consistent with gastritis.

DR. EMERY: Are these the dilated veins?

DR. ROBBINS: I doubt if one can recognize a dilated vein 3 mm. in diameter. At the last examination the distal portion of the cap remained narrow.

DR. EMERY: It was not very constricted.

DR. ROBBINS: As you see it is fairly narrow and does not open up to normal width. I see nothing that suggests polyp in the stomach.

DR. EMERY: Am I right in believing that these findings are not characteristic of duodenal ulcer?

DR. ROBBINS: Certainly there is no positive evidence of a crater. It is only suggestive of one.

DR. EMERY: At the end of the second week in the hospital a gastroscopy revealed what, to me at least, is an unusual condition, namely, a network of dilated veins, 1 to 3 mm. in diameter; they were covered with a rather smooth, slightly reddened mucosa and were situated on the anterior wall, extending from the angulus to the cardia. This is an unusual finding and I am not entirely clear from this description just what the condition suggested. If Dr. Edward B. Benedict is here I hope that he will tell us a little more about it. Offhand, it makes one think of an increase in portal pressure, but so far we have nothing else to go with such a condition. It is not my idea of a spider angioma, which, of course, is a cause of frequent and severe bleeding in the gastrointestinal tract. Usually one makes the diagnosis of this condition by finding evidence for it in either the pharynx or larynx, but no mention of any such finding is made.

Schindler² reports having seen dilated veins in only one case and that patient had a carcinoma of the pancreas that was compressing the portal system. He did not state whether esophageal varices were also present. I do not know whether such a condition can be caused by an allergy, although it seems unlikely.

DR. J. H. MEANS: The abstract gives a false impression of Dr. Benedict's findings. I saw this man on the last admission and struggled a great deal, diagnostically speaking. At the first gastroscopic investigation Dr. Benedict found what he believed to be gastric varices but no evidence of esophageal varices. The second gastroscopic examination was different. The findings were consistent with gastric atrophy, and he doubted that the patient had real gastric varices.

The reason the patient spent nineteen years in the Philippines is that he was a Philippino.

DR. EMERY: The patient was discharged against advice but readmitted five months later, having continued to bleed off and on in the interim. The essential findings on the second admission were an

anemia of 3,100,000, a hemoglobin of 7 gm. and a white blood-cell count compatible with this anemia. The serum protein was again elevated, as already mentioned. In addition, a cephalin-flocculation test was \pm in twenty-four hours and $++$ in forty-eight hours, which, to my way of thinking is essentially negative. After several transfusions the patient was explored on the twenty-first hospital day.

In trying to evaluate this case the first question to settle is whether this man had a duodenal ulcer. This we shall have to decide on the basis of the pain radiating through to the back and the intermittency of the distress. It could have been duodenal ulcer, but it was certainly not characteristic of duodenal ulcer. Gastroscoy suggested trouble in the anterior wall of the stomach and, at one time, dilated veins. A later gastroscoy gave the impression of atrophy of the mucous membrane. One thing against ulcer is the somewhat atypical x-ray picture after thirteen years of the trouble. If ulcer was present, could it have explained the peculiar nature of the veins in the stomach? Ulcers, of course, can be responsible for large amounts of bleeding. The general history, the fact that this patient was allowed to go for so long a time without surgery and the fact that the case is being presented for a clinicopathological conference all suggest, however, that something else was responsible for the bleeding.

It is hard for me to believe that this man had a fungus infection for fourteen years. So I shall have to rule it out on that basis. How about tuberculosis? If this was tuberculosis of the lung, and I understand that the x-ray findings were compatible with it, a tuberculous infection could have developed in that portion of the gastrointestinal tract and could have produced chronic lesions that might perhaps bleed from time to time. Against it, however, are the location and the fact that it would be extremely uncommon for tuberculosis to produce as much bleeding as this man had. Although we see tuberculosis around the duodenum at times, the commonest place is in the ileocecal region.

Could the bleeding have been the result of a food allergy? In view of one case that I have observed, it would seem as though it could. This patient was a man of twenty-five who had always suffered from hives on eating certain foods. For some time before we saw him, he had suffered from hunger pains. He entered a hospital because of a recent attack of severe bleeding, which lowered his red-cell count to 2,500,000. Further observations on the part of the physicians and the patient revealed that three conditions were necessary to produce the bleeding: that he eat onions, that he eat a heavy meal with them, and that he be nervously tired. Any one of these conditions alone did not seem to bring on an attack, but the combination of all three inevitably did.

Could allergy explain the gastroscopic appearance in this case? There is little in the literature that I have been able to find along these lines. Schindler²

quotes others but does not give any opinion of his own. Almost all gastroscopic observations on allergic individuals confirm the existence of gastritis. The patient of whom I was just speaking had four gastroscopic studies. Three were in England. The first examiner reported a normal stomach; the second, numerous erosions with bleeding; the third, a large wheal where the speculum touched the mucosa, which bled profusely in fifteen seconds. The fourth examination was made at a large medical clinic, where the mucosa was reported as pale and flaccid, suggesting a chronic type of gastritis. At times, a portion of the membrane became edematous, resembling the mucous membrane of a nasal polyp. One wonders whether the first gastroscopic examination in this patient, which was said to have shown a gastric polyp, may have been a similar type of lesion. It is difficult, however, to explain the dilated veins on the basis of allergy. Could these dilated veins have been the result of increased portal pressure? There is no evidence for liver disease or increased portal pressure other than those veins. S. Burt Wolbach told me that he had seen portal stasis as a result of pressure from enlarged lymph nodes, and another physician told me that he had seen a case in which a duodenal ulcer had caused thrombosis of the portal artery, with retrograde flow. As previously stated, Schindler² reports one case of dilated veins in the stomach, which was the result of a pancreatic carcinoma interfering with the portal circulation.

I do not have the slightest idea what this man had, but in order to make a diagnosis I shall guess that he had a duodenal ulcer, acute allergy and portal involvement causing pressure on the veins. It is possible, in view of the experience with this patient just mentioned, that the bleeding was the result of any one of these things, but was caused by a combination of all.

DR. MEANS: I might tell Dr. Emery that, as far as I know, no one made the correct diagnosis of this man until he was explored — neither the physicians nor the surgeons. When I first saw him, at the time of the last entry, I thought he probably had a splenic-vein occlusion in the splenic vein. I was much impressed with Dr. Benedict's gastroscopic report and appointed when he back-watered on the second day to speak. There are other points that we did not emphasize so much as Dr. Emery has, perhaps we should have. The striking thing was the bleeding. The surgical consultant thought that the man had a duodenal ulcer. I thought that he did not have a duodenal ulcer but I did not know what he had, unless it was splenic-vein occlusion. We could find no evidence of tropical disease. He had been in this country for great many years.

DR. ALLAN M. BUTLER: I have just been looking through the record to check the serum protein values. There is little doubt that they were high. The values varied on repeated analysis from 6.5 to 7.5.

gm. per 100 cc. The albumin-globulin ratios, often the case, were not too constant. Errors were readily made in that determination. In one case the protein was 8.5 gm. and the albumin said to be 6.1 gm. and the globulin 2.4 gm. In another the protein was 8.4 gm., the albumin 5.1 gm., and the globulin 4.5 gm. I should tend to

the surface of the bowel. Here the fat was soft, not boggy, and the lesions were of a constricting nature, with a tendency to encircle the bowel. I was called to the operating room before resection and given the story of bleeding over a long period of time, and I therefore suggested that it might be a Kaposi's sarcoma involving the bowel. There were three or

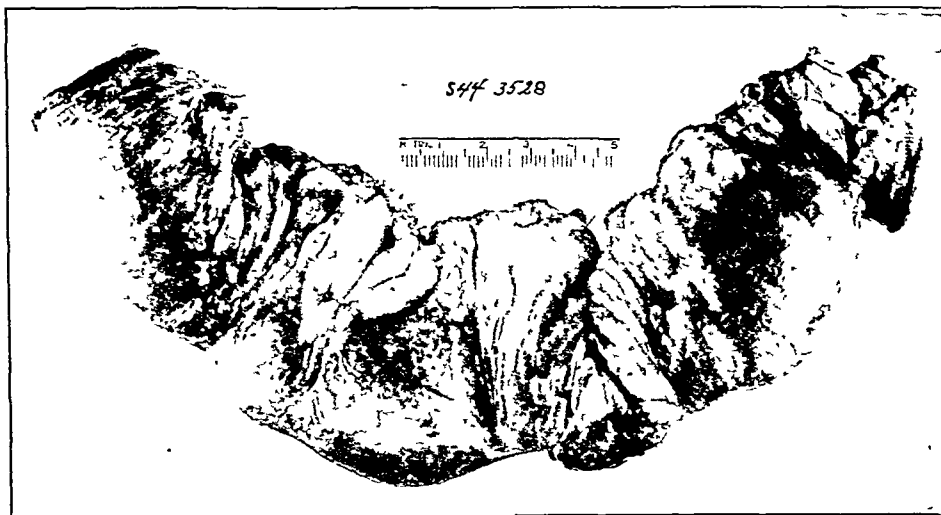


FIGURE 1.

believe the latter values. It seems to me that with repeatedly high protein levels, one has to consider disease in the liver.

CLINICAL DIAGNOSIS

Duodenal ulcer?
Splenic-vein thrombosis?

DR. EMERY'S DIAGNOSES

Duodenal ulcer.
Acute allergy.
Pressure on portal vein?

ANATOMICAL DIAGNOSIS

Tuberculosis of jejunum, ileum and regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr. Leland S. McKittrick operated on this man and was unable to find anything abnormal in the stomach or duodenum. Beginning about 10 cm. from the ligament of Treitz was the first of multiple constricting lesions of the small intestine. The largest lesions were in the proximal 25 cm. of the jejunum and this segment was resected (Fig. 1). The mesentery contained several enlarged nodes, and although the mesenteric fat did not extend very far over the intestine the diagnosis of regional enteritis was considered at operation. In most cases of regional enteritis the fat becomes extremely boggy and extends over

four lesions 2 to 3 mm. in diameter in the ileum, one of which was resected.

When the bowel was opened, the constricting lesions proved to be ulcerations (Fig. 2), and in the gross we thought that the best bet was a regional enteritis. We could not rule out tuberculosis or any other granulomatous process. The microscopic sections showed an acute and chronic process with granulomatous tubercle-like lesions and an occasional giant cell in both the base of the ulcer and the regional nodes. One large node was broken down and suggested caseation. Twenty-five years ago I am sure that most pathologists would have made a definite diagnosis of tuberculosis. Within recent years, however, since Crohn's³ description of regional enteritis and because of the fact that we were unable to find any definite caseation on microscopic examination, we made a tentative diagnosis of regional enteritis. I was examining the slides this morning, not having seen them for a month or so, and the more I looked at them, the more I thought that the process was not characteristic of regional enteritis. I recalled that we had injected some of the material into a guinea pig, and although it was perhaps too early to autopsy the pig, we examined it and found a large node in the groin where the material had been injected. We therefore autopsied the pig and had no difficulty in finding tubercle bacilli in the node. The spleen and the iliac lymph nodes also showed tuberculosis.

Here then is a man who apparently was having chronic bleeding from tuberculosis over a long period of time. I do not recall seeing a similar case. Within recent years we have probably been leaning a little bit too far toward making the diagnosis of regional enteritis when we are confronted with these lesions and rarely consider tuberculosis. It is worth emphasizing the need of guinea-pig inoculation of material from all cases of suspected regional enteritis. The tuberculin test using a dilution of

creasingly weak. Eight months prior to admission he developed extreme urgency and frequency, nocturia ten to twelve times, dribbling and enuresis. The urinary stream was small and intermittent, requiring considerable straining. The urine had a strong odor. He noted a gradually increasing mass in the lower abdomen. Constipation, always a mild one, became severe, requiring Epsom salts or castor oil almost daily, but the stools appeared normal. Six months before entry he developed attacks of pain

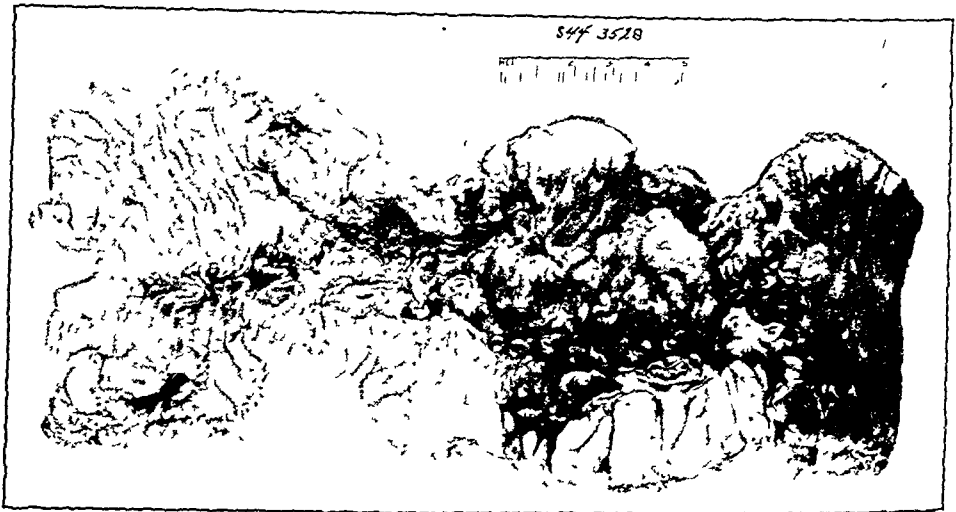


FIGURE 2.

1:50,000 was negative; it should have been repeated using stronger dilutions.

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DR. BUTLER: Dr. William Beckman entered a note in the record suggesting that a granulomatous disease might give a high serum globulin level.

DR. CASTLEMAN: The patient may have had tuberculosis involving the liver at the time of the operation. I do not believe that they examined the liver carefully at that time.

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CASE 30322

PRESENTATION OF CASE

A sixty-five-year-old gardener was admitted to the hospital complaining of a mass in the hypogastrium associated with anorexia and increasing weakness.

Fourteen months prior to admission the patient began to complain of anorexia, associated with nausea and vomiting occurring three or four hours after meals. He acquired a distaste for meat, fish and butter and limited his diet to milk, cereal, toast and an occasional egg. His weight, originally 248 pounds, fell to 177 pounds, and he became in-

creasingly weak. Eight months prior to admission he developed extreme urgency and frequency, nocturia ten to twelve times, dribbling and enuresis. The urinary stream was small and intermittent, requiring considerable straining. The urine had a strong odor. He noted a gradually increasing mass in the lower abdomen. Constipation, always a mild one, became severe, requiring Epsom salts or castor oil almost daily, but the stools appeared normal. Six months before entry he developed attacks of pain

mal nocturnal dyspnea relieved by sitting up and medication furnished by his physician. His ankles began to swell, and he developed dyspnea on exertion. At the time he was told that he had hypertension.

The patient claimed to have had rheumatic fever at the age of six, apparently without sequelae. Except for the fact that one sister had tuberculosis the family history was noncontributory.

Physical examination revealed a pale, thin, appearing man. Venous pulsations were visible in the neck. The apical impulse was felt in the anterior axillary line. Rough apical and high-pitched aortic systolic murmurs were audible. There were frequent premature beats. At the base of the right lung in the left axilla, there were flatness to percussion, crackling rales were present. Over the lower thorax of the left chest posteriorly, and to a higher level in the left axilla, there were flatness to percussion, absent tactile fremitus and markedly diminished breath sounds. A nontender, symmetrical, smooth, cystlike mass measuring about 15 cm. in diameter was palpable in the hypogastrium, its upper border reaching a point 5 cm. below the umbilicus. The prostate was markedly enlarged, the right lobe being somewhat larger than the left, and a No. 20 Foley catheter could be passed only with difficulty. There was marked pitting edema of the legs up to the thighs and over the sacrum. The radial vessels were tortuous and very firm. The fundi showed advanced arteriosclerotic changes.

blood pressure was 234 systolic, 84 diastolic. Temperature was 97.6°F., the pulse 70, and the respirations 20.

Red-cell count was 2,180,000, with 6.8 gm. of hemoglobin. The white-cell count was 4600, with 65 per cent neutrophils. A catheterized urine specimen revealed a specific gravity of 1.008 with a negative test for albumin, and contained innumerable red cells, with 8 to 10 white cells and an occasional per high-power field. The serum nonprotein nitrogen was 142.5 mg. per 100 cc. The serum protein was 5.6 gm. per 100 cc., with an albumin-globulin ratio of 2.2. The fasting blood-sugar level was normal. The blood chloride was 109 milliv. per liter, and the carbon dioxide content 14.3 equiv. A blood Hinton test was negative.

Röntgenographic examination of the chest revealed a considerable amount of fluid in the left pleural cavity. The portions of the lungs unobscured by fluid appeared clear. The heart was not remarkable, but the left border was not distinctly demonstrated. A gastrointestinal series revealed some distention of the duodenal cap but no definite ulcer was seen. A barium enema was negative.

The bladder was catheterized, and 500 cc. of urine was withdrawn, following which the abdominal mass disappeared. Constant bladder drainage was instituted. The patient was also given digitalis and placed on a low-salt diet with a daily fluid intake of 2000 cc. orally. On this regime the sacral edema disappeared and the pleural effusion greatly diminished.

On the eleventh hospital day, on getting out of bed, the patient felt faint and everything "went black." He was put back to bed, where he complained of a severe persistent substernal pain. At that time the blood pressure was 160 systolic, 60 diastolic. An electrocardiogram revealed slight ST-segment inversion of T₁ and CF₅, a diphasic T₂, and an upright T₃, CF₂ and CF₄. This was thought to be consistent with either hypertensive or coronary heart disease, or both, but there was no evidence of recent infarction. A portable x-ray film of the chest was unsatisfactory. At that time there was slight tenderness of both calves but no ankle edema.

In the ensuing days, the patient continued to feel weak and faint, complained of persistent epigastric and substernal pain and began to hiccough. The blood nonprotein nitrogen, which had fallen to 87 mg. per 100 cc. on the fourteenth hospital day, began to rise again, gradually reaching 125 mg. The urinary output diminished in spite of a daily fluid intake of more than 2500 cc. The urine had a specific gravity of 1.010, with a + to ++ test for albumin and innumerable white cells. The patient became increasingly lethargic and had constant episodes of retching. On the twenty-second hospital day the temperature rose to 100.2°F. Two days later, the breathing was loud, labored and bubbling, with bronchial breath sounds and numerous coarse rales throughout the chest. A pericardial friction rub and diastolic gallop rhythm

appeared. The patient died on the twenty-fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. MARIAN ROPES: In this case, as is true in the cases of many patients of this age, a single diagnosis is not adequate to explain the picture. Several disease processes are apparent with manifestations that were typical, but other changes are hard to explain. I shall start with the more obvious ones.

The patient had hypertension and advanced arteriosclerosis. I assume that the heart disease and the resulting congestive failure were on that basis. In view of the story of rheumatic fever in the past it is impossible to rule out underlying rheumatic heart disease, although there is little evidence for this aside from the fact that an apical murmur of rough quality is more consistent with rheumatic than with arteriosclerotic heart disease; on the other hand, a high-pitched aortic murmur is equally consistent with rheumatic and arteriosclerotic heart disease. I believe, however, that the involvement of the heart was not the primary factor in the picture and was not directly related to the rest of it, except in so far as the severe congestive failure affected the other diseases present, such as renal failure. The pleural effusion on the left I assume to have been secondary to congestive failure. Unilateral effusion resulting from congestive failure occurs on the right side in the majority of cases, but on the left it is not uncommon. The possibility of underlying cancer or tuberculosis has to be considered in view of the rest of the picture.

One other definite fact is a disturbance of the genitourinary tract. The patient had definite prostatic hypertrophy. Not much information is given and it is difficult to determine whether it was benign hypertrophy or cancer of the prostate. I am assuming that it was the former. He surely had urinary infection, which was increased if not originally caused by the obstruction to the outflow of urine from the bladder. The sudden appearance of evidence of obstruction and infection at the same time, however, suggests that infection by the inflammatory reaction it caused at least played a role in the obstruction. Subsequently the patient developed renal failure, in which various factors must have played a role. There was an element of vascular nephritis, although it is difficult to determine the degree. The congestive failure presumably played some role, but without doubt the infection and the obstruction were the most important factors.

Beyond that, the picture becomes less definite. The onset of the illness, with gastrointestinal symptoms, and the subsequent loss of weight and weakness six months before evidence of cardiac failure and of renal disease suggest that these were not directly related to either cardiac failure or renal disease. They do suggest, however, the presence of some underlying disease, which I think was probably cancer, although tuberculosis must surely be kept in mind. The gastrointestinal symptoms

Here then is a man who apparently was having chronic bleeding from tuberculosis over a long period of time. I do not recall seeing a similar case. Within recent years we have probably been leaning a little bit too far toward making the diagnosis of regional enteritis when we are confronted with these lesions and rarely consider tuberculosis. It is worth emphasizing the need of guinea-pig inoculation of material from all cases of suspected regional enteritis. The tuberculin test using a dilution of

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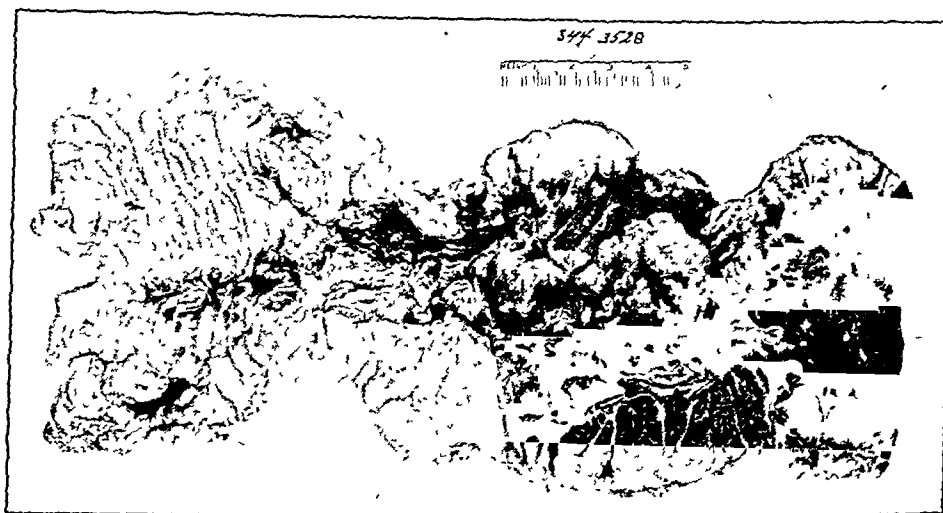


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THE MEDICAL OFFICER

SURGEON GENERAL KIRK¹ has said, "The human relationship of the doctor, patient and family cannot be laid aside with the donning of the uniform," and Colonel Herrman L. Blumgart,² addressing the members of the graduating class of the Harvard Medical School in December, 1943, emphasized this point when he quoted the legendary exclamation of the soldiers of Charles the Fifth: "We have no longer any fear to die, even if we should be wounded. Paré, our friend, is among us."

Yet such counsel is not always heeded, and there are, unfortunately, a small number of medical officers in the armed forces who have

adopted in their care of the sick and wounded a degree of callousness well calculated to arouse just resentment. Such an attitude on the part of a medical officer, rare though it is, may well cause dislike not only of the physician involved but also of the service of which he is a part. It is possible that such an attitude is fostered by misinterpretation of the rarely heard admonishment, "Remember that you are an officer first, a doctor second." A high-ranking medical officer of the Army, — a man of great experience and with many years of service to his credit, — when asked if a doctor entering the service should adopt such a motto, replied, "If he does, Sir, he may make many enemies."

Every physician in civil life knows that a certain degree of detachment from a patient's plight must be developed if one is to retain one's objectivity. Every officer of the armed forces realizes that there are times — they may be few or they may be many — when his rank must come to the forefront of the situation. Every medical officer knows — as does his civilian counterpart — that there are times when one must crack down on a patient and perhaps be temporarily harsh. But it is well to remember that, as one medical officer of the Navy has said, "a sick or wounded fighting man has something that is just too big for him to handle, and unless he can repose his confidence and faith in you, there is but little to which he can look forward."

To physicians about to enter the armed services — indeed to those who already are medical officers — it might appropriately be said: see to it that neither the strain of battle nor the fatigue of long hours nor the tedium of inactivity nor the restiveness of being in a comparatively minor post nor anything else deter you from the just and proper care of the sick and wounded soldier. Is he — whether wounded, ill or malingering — fundamentally different from his counterpart in civil life? Only in these respects: he is far from home; he is doing something that he does not like; and he may well have been through living hell.

A hospital corpsman who landed with the first Marines on Guadalcanal closed his excellent discussion of this subject with these words: "I have my morphine and I have my tourniquet and my kit, and when I hear the cry 'Corpsman,' I creep up

suggest either direct or indirect involvement of that tract.

This may be a good time to look at the gastrointestinal x-ray films. I judge that they show very little.

DR. MILFORD SCHULZ: They were negative.

DR. ROPES: There was no mass or evidence of extrinsic pressure?

DR. SCHULZ: Nothing.

DR. ROPES: Before attempting to put this together I should like to mention the attack of faintness and precordial pain on the eleventh hospital day. Various possibilities are suggested, such as coronary thrombosis, pulmonary infarct and hemorrhage. The subsequent course and findings, however, do not seem to support any of these. It is possible that the pain was caused by the pericarditis, of which there was evidence later in the form of a friction rub. This I assume was due to uremia. I also assume that the majority of the terminal symptoms were associated with the combination of cardiac failure and renal failure.

In attempting to sum this up, I am sure that this patient had hypertensive and arteriosclerotic heart disease with congestive failure and, terminally, pulmonary edema, presumably not related to the rest of the picture. I also believe that he had benign hypertrophy of the prostate. He certainly had a urinary-tract infection, with obstruction and renal failure, and died in uremia. I also believe that he had some underlying disease, but I find it hard to place, except that it involved the abdomen. It was probably a malignant tumor, the nature of which is not clear. I should guess that it arose primarily in the gastrointestinal tract, although there is little evidence for that. Possibly the genitourinary tract was involved.

DR. WILLIAM C. QUINBY: May I ask why you feel that there must have been some other cause? May not the renal difficulty have accounted for the digestive troubles in the beginning?

DR. ROPES: I thought that the digestive troubles and the loss of weight were out of proportion to the other evidence of renal abnormality.

DR. QUINBY: In my experience it is not uncommon to find an old gentleman coming in complaining of dyspepsia in whom the whole thing is due to an overfull bladder, which he does not realize is present. After the urinary tension is relieved, whether or not he gets well depends on the renal function. I really do not believe that one has to assume that this patient had a malignant tumor in the gastrointestinal tract.

CLINICAL DIAGNOSES

Arteriosclerotic and hypertensive heart disease.

Chronic vascular nephritis.

Uremia.

Prostatic hypertrophy.

DR. ROPES'S DIAGNOSES

Hypertensive and coronary heart disease, with congestive failure.

Pulmonary edema, terminal.

Benign prostatic hypertrophy.

Urinary-tract infection.

Uremia.

Malignant tumor of gastrointestinal tract?

ANATOMICAL DIAGNOSES

Prostatic hyperplasia.

Bronchopneumonia: left lower lobe.

Empyema, left.

Dilatation of bladder.

Hydroureter, bilateral.

Chronic pyelonephritis, slight.

Chronic vascular nephritis.

(Uremia.)

Cardiac hypertrophy.

Coronary sclerosis.

Rheumatic heart disease, with mitral and aortic stenosis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this man showed an enlarged heart, which weighed over 500 gm. There was no pericarditis. The coronary arteries were severely diseased, but no definite occlusion or infarction could be found. There was moderate rheumatic involvement of both the mitral and aortic valves, with slight calcareous aortic stenosis. In the left pleural cavity there was a liter of turbid, fibrinous fluid surrounding the lower lobe, which was completely solid; on section the consolidation was proved to be due to a confluent bronchopneumonia. I believe that the pneumonia and pleurisy began at the time that the patient had the severe chest pain.

Since there was no pericarditis, the friction rub must have been pleural in origin.

The kidneys together weighed 200 gm. and in gross showed a slight degree of vascular nephritis. Microscopically there were mild vascular changes and some evidence of pyelonephritis. The kidneys on examination would never lead one to believe that this patient had uremia with a nonprotein nitrogen of 140 mg. per 100 cc. He did, however, have some degree of pyelonephritis resulting from the large prostate, which had produced urinary retention. The bladder was markedly distended and trabeculated, and the ureters were slightly dilated.

I believe that a combination of factors produced death. He had a rather severe bronchopneumonia with early empyema, an enlarged decompensating heart and mildly diseased kidneys — all of which combined to put him into a mild state of uremia.

There were also a slightly thickened gall bladder and gallstones, which I do not believe played any role. The gastrointestinal tract was normal, and the enlarged bladder, as Dr. Quinby suggested, probably accounted for the digestive symptoms.

DR. ALLAN M. BUTLER: Would you agree that the prostatic obstruction was the factor in initiating the changes leading to this man's death?

DR. CASTLEMAN: Yes.

food rationing, price administration, sales taxes, travel priorities, labor control and the highest taxes in its history can also do without one other luxury item — an item that millions of its people have never even seen. And while we are not at it, if we have the courage to be about it, let us remove various other loads from the overburdened physician. Let us take away from him the burden of being considered the proper person to decide who is entitled to extra gasoline, for health reasons, or to extra fuel oil on the same basis. Where decisions of this nature are to be made on medical grounds, let medical panels be appointed to make them, without fear or favor. Let us try this time to rescue the doctor from the uncomfortable position that he occupied during the rousing days of prohibition.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

WHITMARSH — Willard F. Whitmarsh, M.D., of Bridgewater, died May 15. He was in his eightieth year. Dr. Whitmarsh received his degree from Harvard Medical School in 1891. He was a member of the American Medical Association.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT

NEEDS OF PUBLIC HEALTH SERVICE

The United States Public Health Service needs 322 physicians immediately. About 170 of these are required for assignment in the War Shipping Administration, for foreign shore duty with the United Nations Relief and Rehabilitation Administration and for sea and foreign shore duty in the United States Coast Guard. The remainder are needed for duties in the Hospital Division, foreign quarantine, tuberculosis control, venereal-disease control and other state control activities.

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The work on the biochemistry of synaptic transmission of the nerve impulse is fully considered. It is now known that acetylcholine is found in large amounts at the myoneural junction and that it effects the transmission of the nervous impulse across the synapse. This chemical, moreover, is controlled by enzymes — choline esterase, acting to destroy, and choline acetylase, a synthesizing agent. There is therefore a fine balance of a biochemical nature at the junction and, indeed, the same process or a similar process may go on at every point in the nervous system where two neurones are bridged by a synapse. These problems and others now in

on my belly hoping to God that the boy isn't dead before I get there and hoping to God I don't get killed before I reach him, and I give him the morphine and use my tourniquet if it's needed. And I ask you, doctor, What more is there left except encouragement and understanding and tact and the giving out of hope and the gaining of confidence?"

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1. Kirk, N. T. A personal message from the Surgeon General. *Army Med. Bull.* 68:248, 1943.
2. Blumgart, H. L. The doctor as medical officer in the armed forces *Harvard Med. Alum. Bull.* 18:78-81, 1944.

STRADDLING THE ISSUE

ONE interdiction, promulgated by those who watch sleeplessly over the Nation's welfare, that seems to have made little impression on the conscience of the country is the ruling of the War Food Administration relating to the use of heavy cream. Despite the apparent need for the conservation of our milk supply, this regulation, barring from retail sale, except on the prescription of a physician, cream containing more than 19 per cent of butterfat, seems to have acquired in the minds of many the status of an unpopular sumptuary law, possessing neither moral justification nor patriotic appeal.

An investigation has been made into the indispensability of heavy cream in the treatment of the sick, and no competent authority has been cited who is willing to champion any dietary need that cannot be met by the use of 19-per-cent cream with other fats. The Subcommittee on Medical Food Requirements of the Committee on Drugs and Medical Supplies of the National Research Council has denied the indispensability of this form of food; the Council on Foods and Nutrition of the American Medical Association has shown its use to be limited to the production of a ketogenic diet, and has admitted that this diet can be attained satisfactorily by the use of butter, salad oils and cream of the permissible fat content. Chiefs of various hospital services have disclaimed heavy cream as a necessary dietary adjunct; the Boston Medical Milk Commission has declared that its value in medical treatment is unimportant. And yet, according to the *Journal of the American Medical*

Association,* available evidence indicates during the past winter, in New York City, the equivalent of 500,000 quarts of milk went into heavy cream on doctors' prescriptions!

The *Journal of the American Medical Association* suggested a partial remedy for the situation. The War Food Administration has, unfortunately, not accepted the suggestion, which was put into effect as of August 1. The suggestion provides for the endorsement of the physician's prescription for heavy cream by such an official as the health officer or the secretary of the county medical society; the amendment of the War Food Administration reconstructs the suggestion, leaving it the approval of the physician's prescription to the public health officer, or the secretary of the county medical society, of the municipality or county wherein such patient resides." First, the doctor is entrusted with an entirely superfluous responsibility, and then his medical colleague, or perhaps the local druggist, undertaker or carpenter, by virtue of his membership on the local board of health, is set as a watchdog over him!

This new gratuitous irritation seems to be a rather ill-considered way for an earnest, conservative governmental agency to avoid an issue. If there is a real need for the conservation of milk, — and we are constantly told that it exists, — and with heavy cream authoritatively declared to be a negligible factor in the treatment of illness, why, in all conscience, cannot this unnecessary luxury be withdrawn entirely from circulation instead of the doctor being again made the whipping boy, this time for cream to whip!

In Massachusetts, fortunately, this situation has undergone considerable amelioration through the farsightedness and energy of the state director of War Food Administration. This official, unable to obtain rescindment of the amendment, has obtained permission to place his own interpretation on its contents. By this interpretation a committee has been appointed to function in place of the variegated officers originally designated to approve the doctors' prescriptions.

Certainly a democracy at war that can accept selective service, tire confiscation, gasoline, fuel

*Editorial. Prescription of cream for the sick. *J. A. M. A.* 124:511, 1944

food rationing, price administration, sales taxes, travel priorities, labor control and the highest taxes in its history can also do without one other luxury item — an item that millions of its people have never even seen. And while we are at it, if we have the courage to be about it, let us remove various other loads from the overburdened physician. Let us take away from him the burden of being considered the proper person to decide who is entitled to extra gasoline, for health reasons, or to extra fuel oil on the same basis. Where decisions of this nature are to be made on medical grounds, let medical panels be appointed to make them, without fear or favor. Let us try this time to rescue the doctor from the uncomfortable position that he occupied during the rousing days of prohibition.

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the forefront of physiologic thought are fully elucidated in this new edition. Professor Fulton has called on many experts, particularly qualified in special fields, to aid him, and their material and the results of his own researches are integrated into each chapter by the author.

The reviewer believed that the first edition of this work was an outstanding contribution to the subject; his opinion is reinforced by the appearance of the second edition, so thoroughly revised and brought up to date. The book can be highly recommended to medical students, physicians and workers in laboratories and libraries. It is, indeed, a fundamental text that should find a place on the shelves of all medical libraries both public and private.

Lectures on Peace and War Orthopedic Surgery. Selected from the instructional courses presented at the eleventh annual assembly of the American Academy of Orthopaedic Surgeons, Chicago, January 17, 18, 19, 20 and 21, 1943. Edited by James E. M. Thomson, M.D. 4°, cloth, 322 pp., illustrated. Ann Arbor, Michigan: Edwards Brothers, Incorporated, 1943. \$4.00.

Usually papers that are read in medical meetings do not have a prolonged appeal or arouse sufficient interest to warrant their separate printing in book form. But here is an exception. This book, a résumé of instructional courses in the orthopedic surgery of war given at the 1943 meeting of the American Academy of Orthopedic surgery, is timely and practical. Dr. James E. M. Thomson has edited the volume in a commendable manner. It is unfortunate that a few of the speakers failed to provide a synopsis of their talks. The book is well illustrated throughout. It is recommended as a valuable addition to the library of those interested in orthopedic surgery.

Gastro-Enterology (in three volumes). By Henry L. Bockus, M.D. Volume 1: *The esophagus and stomach.* 4°, cloth, 831 pp., with 134 illustrations and 21 tables. Philadelphia and London: W. B. Saunders Company, 1943. \$12.00.

This is an excellent book, probably the best on the subject in the last ten years. It is no simple compilation; the opinions are based on the author's large experience. It is well written, interesting and unusually complete, and unlike some books of its size it is not loaded with laboratory methods and types of treatment that are obsolete and have only historical value. It is fully illustrated. The x-ray illustrations are of especially high grade, being clear and definite and having a real purpose, which is a delightful contrast to some of the older textbooks. A great number of well-chosen references are found at the end of each chapter. Habits and fads in diagnosis and treatment are absent; in fact, there is a short section entitled "Avoidance of Enthusiasm for Certain Procedures."

Many controversial subjects, such as the etiology of peptic ulcer, the mechanism of its pain, its transformation into cancer, the value of gastroscopy and its relation to roentgen diagnosis, the relation of gastritis to peptic ulcer and cancer, the best antacids, the treatment of hematemesis by diets, transfusion and operation, and syphilis of the stomach, are treated with good judgment and skill.

The chapters on history taking, histology and physical examination are excellent. Modern methods of examination, such as "spot" roentgen films, gastroscopy, and peritoneoscopy, are freely used and discussed. The author uses the oral tube and fractional gastric analysis by choice, with eight or nine sets of analyses in each case over a two-hour period. Many gastroenterologists still prefer the nasal tube and will not agree that simple examination of fasting contents, with a single test of secretion, "has gradually gone into disuse." The microscopic examination of gastric contents covers ten pages with twenty-three illustrations. This seems rather elaborate in view of its lessened importance in recent years. The Einhorn string test is obsolete and uncertain and could be omitted, also the Woldman phenolphthalein test. The reader is referred to a textbook on laboratory technic for simple tests of the gastric contents. In a book of this size, simple tests for occult blood, lactic acid and so forth could be easily included.

Instead of a fifty-page chapter on roentgenologic examination of the stomach, excellent illustrations and comment are scattered through the book under different diseases. The chapter on gastritis is a great improvement on those

written before the common use of the semiflexible gastroscope. The familiar forty-page chapter on gastric neurosis conspicuous by its absence. There is a good discussion of pain, discomfort, anorexia, bloating and vomiting, nervous or reflex origin under the chapter on syphilis. It is not quite clear why diaphragmatic hernia and hiatal hernia are described separately.

The discussion of peptic ulcer is very complete, taking about 40 per cent of the volume and covering etiology, diagnosis and medical and surgical treatment. Discussion of antacids is particularly useful. Perhaps the variability of magnesium trisilicate preparations should have been mentioned. The chapter on the complications of ulcer and the results that sometimes follow surgery are especially good. The illustrations of many types of gastric tumors are excellent. Syphilis of the stomach is conservatively described.

All in all the book is of high quality and can be heartily recommended.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Medicine and the War. Edited by William H. Taliaferro, B.S., Ph.D. 8°, cloth, 193 pp., illustrated. Chicago: University of Chicago Press, 1944. \$2.00.

This volume comprises a series of ten lectures by the members of the faculty of the Division of Biological Sciences, University of Chicago. These lectures were sponsored by the Charles Walgreen Foundation and although originally prepared for students, are applicable to the needs of the layman. They deal specifically with food in the war, chemotherapy, malaria, insects, disease, and modern transportation, shock and blood substitutes, aviation medicine, neurologic effects in cerebral injuries, psychiatry in the war, and chemical warfare.

The Health of Children in Occupied Europe. A pamphlet published under the auspices of the International Labour Office. 8°, paper, 37 pp. Montreal: International Labour Office, 1943. 25 cents.

This pamphlet provides a preliminary outline for the study of the effects of war on the health of children. The area covered comprises all the occupied countries of Europe.

NOTICES

HARVARD UNDERGRADUATE ASSEMBLY

The annual undergraduate assembly of the Harvard Medical School will be held in the amphitheater of Building E from 2:30 to 6:00 p.m. on Tuesday, August 29. The program will consist of eight student papers on original clinical and laboratory investigation, followed by an address at 5:00 p.m. by Dr. William T. Salter, professor of pharmacology, Yale University School of Medicine, whose subject will be "Drugs as Biologic Catalysts."

Medical students and physicians are cordially invited to attend.

AMERICAN CONGRESS OF PHYSICAL THERAPY

The twenty-third annual scientific and clinical session of the American Congress of Physical Therapy will be held September 6 to 9, inclusive, at the Hotel Statler, Cleveland. The annual instruction course will be held from 8:00 to 10:30 a.m. and from 1:00 to 2:00 p.m. during the days of September 6, 7 and 8. The scientific and clinical sessions will be given on the remaining portions of these days and evenings. All these sessions will be open to the members of the regular medical profession and their qualified aids.

For information concerning the instruction course and program of the convention proper, address the American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago 2.

(Notices continued on page xxvii)

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AUGUST 17, 1944

Number 7

DELIRIUM TREMENS*

CARLETON B. CHAPMAN, M.D.†

BOSTON

THE diagnosis and treatment of delirium tremens are usually considered to lie entirely within the province of the psychiatrist; yet the responsibility for the immediate therapy of the condition frequently falls on the general practitioner or internist. To the psychiatrist delirium tremens is an acute toxic psychosis precipitated by prolonged and excessive drinking of alcoholic beverages by persons who perhaps already possess more or less serious psychiatric abnormalities. To the present-day internist it is essentially a problem in sedation, rehydration and vitamin-replacement therapy, whereas to the chronic alcoholic patient it is a terrifying and sometimes fatal hallucinatory illness. Thus, although the nature of delirium tremens and its long-term therapy are essentially psychiatric problems, a practical knowledge of the disorder and its treatment definitely merits the attention of the internist.

DEFINITION AND DIAGNOSIS

In defining delirium tremens, one can hardly do better than consider the layman's expressive term for the disease, namely, "the shakes and the horrors." Practically, the fully developed condition involves several elements, including chronic alcoholism, nervousness, sleeplessness and tremors, and visual hallucinations, occasionally accompanied by other types of hallucinatory experiences. Clinically, one must recognize the incipient as well as the active phase of the disease. In the incipient stage, only tremors and apprehension are noted. With the addition of hallucinations, full-blown delirium tremens is present. Experienced chronic alcoholic addicts are fully cognizant of the incipient phase, "the shakes," and often seek hospitalization soon after its onset in the hope that they can, by means of medical attention, avoid "the horrors." If proper therapy is instituted at this time, the physician is frequently able to spare the alcoholic patient the

truly frightful experience of fully developed delirium tremens. Furthermore, whereas fatalities among the incipient or prodromal group are rare, the same cannot be said for the full-blown condition.

There are several other types of alcoholic psychoses that may easily be confused with delirium tremens. The interesting and excessively rare condition known as alcoholic hallucinosis usually occurs in a younger age group than does delirium tremens, is associated with auditory hallucinations and not generally with visual hallucinations, and is remarkable in that characteristically the patient's insight into his condition is extremely clear. According to Bleuler,¹ such patients are deeply impressed by the content of their auditory hallucinations but paradoxically often recognize them as false sensory perceptions. Only 1 patient with what appeared to be pure alcoholic hallucinosis was admitted to the Second and Fourth Medical Services of the Boston City Hospital during 1941. Delirium tremens may apparently be superimposed on Korsakow's psychosis, but diagnosis of the latter must await clearing of the delirium.

"Rum fits," perhaps better known as "alcoholic epilepsy," are often associated with active delirium tremens but are probably not a manifestation of that condition per se. Finally, various complex and undiagnosable combinations of the alcoholic psychoses are occasionally seen. Such terms as "alcoholic deterioration" or simply "alcoholic psychosis" are not infrequently employed for discharge diagnoses of these cases.

GENERAL INCIDENCE AND MORTALITY

Accurate statistical information on delirium tremens is difficult to obtain. Moore and Gray's² report indicated that 6.2 per cent of the 38,376 patients admitted to the Boston City Hospital for alcoholism in the twenty-year period ending in 1935 had delirium tremens. In the six-year period, from 1936 to 1941, following this report, there were 14,276 admissions for alcoholism to the same hospital, and of these patients 2985, or approximately 21 per cent, were diagnosed as having delirium tremens.

*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.

†Formerly, assistant in medicine, Harvard Medical School, and resident physician, Second and Fourth Medical Services (Harvard), Boston City Hospital.

All these figures are, however, based on discharge diagnoses made by a great many different staff members, and include incipient as well as active cases of delirium tremens. The 1941 figures for the Second

TABLE 1. *Incidence and Crude Death Rates for Patients with Delirium Tremens on the Second and Fourth Medical Services of the Boston City Hospital in 1941.*

DIAGNOSIS	NO OF CASES	NO OF DEATHS	MORTALITY
Alcoholism	575	—	%
Delirium Tremens	185	9	4.8 (± 1.4)
Incipient	121	0	0
Active	64	9	14.0 (± 4.4)

and Fourth Medical Services at the Boston City Hospital, based on a personal survey of the case records, appear in Table 1.

A summary of crude death rates for delirium tremens in the literature appears in Table 2. Examination of such data discloses several factors of interest. Moore's⁴ figure is actually an average mortality rate for a twenty-one-year period. The rate for the first year of this period reached the astounding peak of 52 per cent, whereas that for the last

TABLE 2. *Crude Death Rates for Patients with Delirium Tremens, as Reported in the Literature*

AUTHORITY	YEAR	DEATH RATE
Ranson and Scott ³	1911	37.0
Moore and Gray ⁴	1915-1935	24.0
Bowman et al. ⁵		
First period	1939	16.0
Second period	1939	4.6
Piker and Cohn ⁶	1937	5.3
Rosenbaum et al. ⁷	1940	1.3

year was 14 per cent. Such an average value thus gives little indication of the current mortality. The studies of Rosenbaum et al.⁷ do not include cases having serious complications such as trauma and pneumonia, and their death rate is based on cases of active delirium tremens only. In Table 1, death rates for active delirium tremens and for the total group are given, the latter figure, 4.8 per cent, being roughly comparable with Moore's figure of 14 per cent. No attempt was made to rule out the cases in our series that were complicated by serious illness other than delirium tremens.

AGE, SEX AND RACE INCIDENCE

Active delirium tremens is most frequent between the ages of forty and fifty.⁸ In this series the peak incidence occurred between the ages of thirty and fifty, as shown in Table 3. It may be inferred from the figures in this table that delirium tremens does not develop until constant and heavy alcoholic indulgence has extended over many years. Close consideration, however, indicates that the peak incidence for chronic alcoholism, as reported by Moore,² coincides with that for delirium tremens,

so that conclusions from such figures as to the length of time required for the development of delirium tremens cannot logically be drawn.

Most studies indicate that active delirium tremens occurs far more frequently in men than in women, and the present series, in which only 4 patients, women, is in agreement. This difference is, probably less pronounced than it appears, so

TABLE 3. *Age Incidence in Cases of Active Delirium Tremens Admitted to the Second and Fourth Medical Services of the Boston City Hospital in 1941.*

AGE GROUP	NO OF CASES	PERCENT
20-29	4	6
30-39	20	31
40-49	27	41
50-59	9	14
60-69	4	6
Total	64	

female alcoholic patients are much more likely to be treated at home than on the wards of a public hospital.

It is striking that of the 62 patients with active delirium tremens none were Jewish, in spite of the fact that about 10 per cent of all patients admitted to the hospital are Jewish. The extremely low incidence of delirium tremens among Jews was commented on by Kat et al.,⁹ who found none in their series of 132 cases seen at the Neuropsychiatric Clinic of the University of Amsterdam, a city having a large Jewish population.

PRECIPITATING FACTORS

Chronic alcoholism, as well as gross malnutrition is intimately associated with delirium tremens. Various concepts and definitions of chronic alcoholism and abnormal drinking have been tabulated by Bowman and Jellinek.¹⁰ It is probably not far from the truth to say that the chronic alcoholic addict is one to whom drinking is life's sole essential activity. In Peabody's¹¹ words, "Normal drinkers are those to whom a night's sleep represents the end of an alcoholic occasion; chronic alcoholics are those to whom a night's sleep is only an unusually long period of abstinence." It is important to note that the emphasis placed on the procuring and partaking of alcoholic beverages by the chronic alcoholic addict often precludes normal activity of any kind. Partial or total abstinence from food concomitant with or as a result of chronic alcoholism is the rule. Practically all observers are agreed that trauma and acute infection frequently precipitate active delirium tremens in chronic alcoholic patients. Some 30 per cent of our cases were complicated by serious infection, including lobar pneumonia and bronchopneumonia, pneumococcal meningitis and in 1 case, miliary tuberculosis. Cases complicated by trauma are admitted to the surgical services and are seldom seen on the medical wards. As a com

ing factor in already serious disease, delirium as must certainly contribute heavily to the lethality in such cases.

Table 4 shows clearly the effect of delirium tremens on pneumonia mortality, as reported by Tilghman in Finland.¹² On statistical examination, the differences in mortality between the group of uncomplicated cases of pneumonia and that of cases

holic patient often undertakes some therapeutic measure at this point. He may, and frequently does, increase his alcoholic intake prodigiously in an effort to "quiet his nerves." Self-medication with paraldehyde is an increasingly frequent occurrence. The fact that the drug is used in hospital practice as an effective sedative in delirium tremens, in addition to the fact that it is procurable in most localities without a physician's prescription, is largely responsible for its increasing popularity among chronic alcoholic patients. Many of our patients with active delirium tremens smell strongly of paraldehyde on admission.

The transition from incipient to active delirium tremens is usually gradual unless precipitated by trauma or severe infection. Mental confusion and disorientation often precede actual hallucinations. Usually, short but vivid visual hallucinations appear first at night. Within the next few hours, the hallucinations may become more frequent and more intense until finally the patient is actively and often dangerously delirious. His response to the hallucinations seems to depend to a large extent on their nature and on his emotional and physical make-up. In general, his actions are obviously motivated by terror, and this fact can hardly be overemphasized. Visual hallucinations are the rule; in addition, auditory hallucinations are frequently but not always present. The objects seen are generally tiny and innumerable, and often direct their threatening activities against the patient himself. The misinterpretation of spots on the bedclothes, leading to plucking movements, is justly considered a classic symptom of active delirium tremens. Snakes, alligators, dogs and other animals frequently figure in the hallucinatory experiences of delirium tremens patients. Some patients complain of countless tiny human forms dancing about the room. A recent patient complained that millions of tiny Japanese soldiers were marching across the floor, up the wall and onto the ceiling in order finally to drop on the bed. Some victims refuse to divulge the nature of their hallucinations, dismissing them as "unmentionable." One female alcoholic patient complained of sleeplessness because she was constantly seeing innumerable cash-register keys and hearing them scream the prices of liquors and cheap wines.

Generally, the hallucinatory phase runs its course in two to four days, although tremors may remain as long as two weeks. If the disease is complicated by serious infection, there may be repeated bouts of hallucinations separated by several days of calm. On recovery from active delirium tremens most alcoholic patients make solemn promises never to indulge again, and at this point they are most susceptible to psychotherapy.

Physical examination in the incipient stage invariably discloses a tremulous, apprehensive person, usually begging for sedation and often smelling of alcohol or, less frequently, of paraldehyde. De-

4. The Effect of Delirium Tremens on Mortality from Pneumococcal Pneumonia.*

DIAGNOSIS	MORTALITY			
	ALL CASES	%	BACTEREMIC CASES	%
Complicated pneumococcal pneumonia	39.8	(±1.6)	79.0	(±2.3)
Pneumococcal pneumonia complicated by delirium tremens	71.0	(±7.3)	100.0	(±8.8)

*Figures are those of Tilghman and Finland¹²; no case received either brom or a sulfonamide.

licated by delirium tremens appear to be fully explained. Although no exact information concerning age distribution of the cases of pneumonia complicated by delirium tremens was available, the difference remained significant when generous allowance was made for this important factor.

CLINICAL FEATURES

In all these cases of delirium tremens, there first occurred a bout of relatively heavy drinking and inadequate food intake, usually lasting from two to six weeks. Rarely the history of such a debauch is withheld by the patient, but in most cases no attempt at concealment was made, although the amounts of liquor consumed were often grossly understated. Early morning drinking is suggestive, since it is well known that persons who drink on rising in the morning frequently do so to calm a shaky hand. The actual amounts of alcoholic beverage consumed vary from a pint to several quarts of various types of liquor. The interrogator should accept with skepticism the statements of a chronic alcoholic addict about his drinking habits, and a negative alcoholic history never rules out delirium tremens as a possibility.

The so-called "prodromal features," such as apprehension, tremors and particularly sleeplessness, are usually considered to indicate incipient delirium tremens. Few cases of active delirium tremens fail to pass through this stage, although the history of it may not be forthcoming. Most patients are chiefly concerned with their inability to sleep, and for this reason many chronic alcoholic addicts become habituated to barbiturates. Apprehension usually develops when the patient realizes that he is about to develop "the horrors," particularly if he has been through the experience before. It is this feature that may send him to a hospital, pleading for admission, in the hope that he will escape the hallucinatory phase of his disease. It is of interest to note that the experienced chronic alco-

hydration, marked by a dry, furrowed tongue and loose, flabby skin, is the rule. The reflexes are often hyperactive. Tremors are best seen in the extruded tongue or in the outstretched hands. Gross generalized somatic tremors may be indicative of a shaking chill, pointing in turn to a complicating infection. Careful examination of the lungs, heart and central nervous system should not be omitted in view of the high frequency of complicating infection or trauma. Generally examination of the abdomen reveals nothing abnormal, but occasionally a rigid and extremely tender abdomen is seen. This condition, known in hospital parlance as the "rum belly," may suggest a perforated viscus with generalized peritonitis, intestinal obstruction or almost any acute abdominal catastrophe. It is variously attributed to acute alcoholic gastritis or to acute pancreatitis, but its true nature is not understood.

Laboratory data indicating dehydration of moderate and occasionally of severe degree are found in the majority of cases. Significant elevations of urinary specific gravity, hemoglobin, white-cell counts and nonprotein nitrogen values are frequently observed. Prompt return of these values to normal occurs in most uncomplicated cases on the administration of fluids.

THE THERAPY

Until comparatively recent times, patients suffering from delirium tremens were usually subjected to no particular treatment other than a jail cell and more or less brutal treatment from unenlightened attendants. The mortality resulting from such treatment will never be known, but it must have been appallingly high. With the introduction of more sympathetic therapeutic measures, the mortality appears to have declined. There remains, unfortunately, much folklore and superstition in connection with the disease in the minds both of the public and of physicians. Some of these concepts are harmless, but some are probably dangerous and should be forthwith abandoned.

Alcohol

A practice still prevalent in Europe is treatment of delirium tremens with alcohol because the condition is allegedly precipitated by abstinence. According to Sheps,¹³ some French clinicians administer alcohol by vein if the patient cannot take it by mouth. One of the most powerful arguments against such therapy is the observation of Piker¹⁴ that from 75 to 90 per cent of patients have delirium tremens while still drinking. Many of the patients with active delirium tremens smell of alcohol on entry, having attempted to ward off this condition by heavier and heavier drinking. Sheps¹³ treated 104 chronic alcoholic patients showing evidence of incipient delirium tremens with hydrotherapy, sedatives and nutritional measures. No alcohol was allowed, yet no case developed active delirium tremens. In

the words of Bowman et al.,⁵ "the administration of alcohol, therefore, either to prevent delirium tremens or as a subsequent therapeutic measure, has no basis in fact, and furthermore often presents an unsurmountable psychologic barrier in the further treatment of such patients."

Spinal Drainage

Therapeutic spinal drainage in delirium tremens was first recommended by Steinebach¹⁵ in Germany and was subsequently advocated by Hoppe¹⁶ in this country, apparently because of a supposed increase in cerebrospinal fluid pressure. More recently Piker and Cohn⁶ attributed their excellent results in delirium tremens therapy in part to spinal drainage. They assumed that there is an irritation to the edema of the brain and meninges and an increase in intracranial pressure. Some doubt was cast on this assumption by Rosenbaum,¹⁷ who after performing lumbar punctures in 234 cases of active delirium tremens concluded that 75 per cent of the patients had normal cerebrospinal-fluid pressure. He made the pertinent observation that it is difficult, under the best of circumstances, to achieve sufficient relaxation for accurate pressure readings in patients suffering from delirium tremens, and suggested that in fact even more than 75 per cent of the patients have normal cerebrospinal fluid pressures. Merritt et al.¹⁸ obtained similar results in examining 201 cases of acute alcoholism, including some cases of delirium tremens.

The finding of the so-called "wet brain" at autopsy in patients dying of delirium tremens is the subject of spirited controversy among neuropathologists, and the relation of such a finding to the disease appears to be in doubt. One is, therefore, forced to conclude that spinal drainage has no rational basis in the therapy of the condition. The measure does not actually alter the clinical course has been established by Rosenbaum, Piker and Lederer.⁷ In carefully controlled clinical experiments, neither spinal drainage nor dehydration measures were found to alter the mortality or clinical course of the disease.

Fluid Therapy

Only comparatively recently has the liberal use of fluids in the treatment of delirium tremens been widely recommended. Piker,¹⁹ who in 1937 recommended spinal drainage and dehydration, re-examined the evidence in 1938. In extensive clinical trials, he was unable to establish the usefulness of fluid limitation and concluded by recommending that fluids be neither limited nor forced. He continued, however, to recommend control of cerebral edema by the judicious use of dehydrants. Bowman, Wortis and Keiser⁵ in 1939 took note of the dehydration exhibited in almost all cases of delirium tremens and recommended full hydration with 3000 to 4000 cc. of fluid per day. They observed

the fluid itself may act as a sedative and that ether medication may be unnecessary. Spinal anesthesia, as well as the use of dehydrating agents, has no place in their therapeutic regime. Wortis,²⁰ in an excellent general review of the subject, states the view that dehydration and spinal drainage are unnecessary and that hydration is a logical and valuable adjunct. Laboratory support for these views is furnished by Cohn,²¹ who found that the blood chloride and carbon dioxide-combining power values were almost always low in delirium tremens, whereas the hemoglobin, serum protein and hematocrit values were increased. He logically concluded that the condition should be treated by restoration of fluid and salt to the body.

It therefore seems unwise and illogical to limit fluids and administer dehydrating agents in a condition of which one of the most constant features is dehydration. In addition, such limitation may inevitably be dangerous, particularly in cases complicated by infection.

Medication

Sedative medication is almost always necessary in treating delirium tremens, and sedation is often difficult to achieve. The older literature contains many recommendations for almost all the known sedatives. The one drug that is almost universally recommended is paraldehyde. Most modern writers^{5, 6} agree that this drug is the most innocuous, the most rapidly eliminated and the most uniformly effective of all sedative medicaments in the treatment of delirium. On the other hand, Henderson and Gillespie²² state that paraldehyde may actually increase the degree of delirium. Sperber²³ holds the same view and states that patients may be fully saturated with the drug and still be actively delirious. Apparent confirmation of this view will have been observed by almost everyone who has had experience in the therapy of delirium tremens. Lano²⁴ offers a plausible explanation for this apparent paradox as follows:

Any chemical sedative, including paraldehyde, if given in fragmentary doses or to individuals who have had other chemical sedatives, may enhance delirium. However, if a patient enters the hospital in incipient delirium tremens and an adequate amount of paraldehyde is given to ensure sleep, it does not provoke the delirium. Certain incipiently delirious patients find themselves on the ascending limb of a delirium and at times paraldehyde is ineffective in checking the course of the delirium.

In other words, adequate doses of paraldehyde will control most cases of active delirium tremens but inadequate doses may well be worse than useless. The initial oral dose recommended by Goodman and Gilman²⁵ is 3 to 8 cc., increased to 10 or 15 cc. if necessary. At the Boston City Hospital, it has been found that single oral doses of less than 8 cc. are of little use in controlling patients with active delirium tremens and that larger initial doses

are indicated. It is highly desirable, as stated by Piker and Cohn,⁶ in all cases of delirium tremens to induce sleep as soon as possible. A rational program to this end is to administer an initial oral dose of up to 16 cc., followed as necessary by oral doses of 8 to 12 cc. every hour. If other measures are adequate, the usual case can be controlled on this regime in two to three hours or less. If the oral route of administration is impossible or impractical paraldehyde can safely be given intramuscularly in doses up to 10 cc. Rectal administration of paraldehyde to actively delirious patients has proved difficult and often impossible in our hands. That the intravenous use of paraldehyde in therapeutic doses may be dangerous is indicated in a recent report.²⁶ Finally, habituation to paraldehyde is not rare, particularly among chronic alcoholic patients who have had repeated bouts of delirium tremens. The drug is actually used as an acceptable substitute for alcohol by some such patients. These facts do not by any means contraindicate the use of paraldehyde in the treatment of active delirium tremens, but when the active phase of the disease is relieved, it is wise to abandon sedatives if possible, or to substitute small doses of barbiturates for paraldehyde if some sedative measure continues to be required.

Barbiturates have been employed much less freely in treatment of delirium tremens than has paraldehyde. One objection is that such large amounts are required that the fatal dose may be approached. Nevertheless, if other measures are adequate, many cases of incipient delirium tremens respond very well to frequent subcutaneous injections of luminal sodium in 3-gr. to 5-gr. doses. The drug is obviously useless in the treatment of active delirium. Sperber,²³ however, used intravenous Evipal Sodium (2 cc. of a 10 per cent solution) to good effect in 3 wildly delirious patients. It should not be forgotten that barbiturates given intravenously may cause serious damage to the liver, particularly in alcoholic patients. Nevertheless, Sperber's suggestion has been followed by us to good advantage in a few particularly violent and obstinate cases. The method is particularly useful in quieting patients who have developed active delirium tremens postoperatively or following severe trauma. In such cases operative wounds may be torn open or further trauma may be inflicted unless the delirium is quickly controlled. The judicious use of barbiturates given intravenously appears fully justified under such circumstances. Morphine has been outlawed in delirium tremens therapy for years, largely because it is said to produce or enhance cerebral edema. Certainly there is nothing to be said in favor of its use in this condition. Apomorphine and strychnine are recommended by Lambert⁸ for severe cases of delirium tremens but are not included in more modern therapeutic

regimens. Scopolamine has been largely abandoned in routine therapy because of the uncertainty of its effect.

Vitamin and Dietary Therapy

Since the introduction of thiamine and nicotinic acid into general use, many reports have appeared purporting to show that they are curative in cases of delirium tremens. Suffice it to say that no report of dramatic success with these agents is convincing. Rapid cures in cases of delirium tremens treated with thiamine have been reported by Kiene et al.,²⁷ Cannon et al.,²⁸ who gave thiamine along with glucose and insulin, and Sciclounoff and Flagg.²⁹ It was Hammargren's³⁰ opinion that thiamine therapy in delirium tremens is sufficiently promising to warrant further investigation. Rosenbaum, Piker and Lederer,⁷ in controlled clinical observations on 36 cases of delirium tremens, found that the patients treated with thiamine required less paraldehyde than did the untreated groups. Nevertheless, they observed that two patients who had incipient delirium tremens on entry developed active delirium tremens after forty-eight hours in spite of large doses of thiamine. Jolliffe et al.^{31, 32} found that nicotinic acid produced dramatic cure in certain cases of alcoholic delirium that they distinguish from delirium tremens as "nicotinic acid deficiency encephalopathy." They point out, however, that in delirium tremens per se they do not consider thiamine or nicotinic acid deficiencies to be etiologically specific, nor do they consider these substances to be curative when used therapeutically. Thus one is forced to agree with Rosenbaum, Piker and Lederer⁷ that, once the disease starts, the addition of thiamine, nicotinic acid, liver extract and brewer's yeast does not aid in shortening the illness.

Nevertheless, to withhold generous quantities of vitamins from patients with delirium tremens appears to be shortsighted and academic. It is a matter of common experience that the patients are badly nourished and subject to gross avitaminoses. For this reason it seems desirable as suggested by Jolliffe et al.,³² to correct faulty vitamin intakes in these patients, although dramatic curative results are not to be expected.

It is extremely important to restore patients who have had delirium tremens to adequate dietary intakes as soon as possible. In unco-operative patients, the administration of large quantities of semi-fluid food rich in carbohydrate and protein by stomach tube is of value. Such mixtures should preferably be divided into small amounts, to be given at frequent intervals.

Miscellaneous Measures

Few writers in recent years have failed to condemn the use of restraint in handling delirious patients, although some authorities recognize it as a necessary evil in situations in which nursing care

is limited. It should be emphasized that the experienced physician is apt to attempt to do with restraint what he has failed to achieve withatives and judicious handling of the patient.

Continuous tub baths for the afebrile or slightly febrile delirium tremens patient are recommended and are used in some clinics with excellent results. This type of therapy is rational and doubtless reduces considerably the amount of sedative medication needed in a given case, but it also requires more facilities and man power than are available in an average public hospital.

Ideally, close attention should be paid to the roundings in which a delirious patient is put. It is often bad practice to leave such patients in darkness, since this seems to increase the terrifying effect of hallucinations. Preferably lighting should be subdued but should extend to every corner of the room. Pictures on the wall are apt to provide the patient with further material for hallucinatory processes. Of extreme importance is the fact that the suicidal or homicidal tendencies of some delirious patients make the leaving of glassware and other loose objects in the room distinctly unwise.

Psychotherapy is of undoubted value in many cases of delirium tremens but is beyond the scope of this paper. In assaying the results of treatment, which is often directed at actual cure of chronic alcoholism, it should not be forgotten that a single bout of full-blown "horrors" is sometimes followed by a prolonged period of abstinence, regardless of the therapy employed. In rare cases, a vigorous bout of delirium tremens may afford sufficient impetus to induce a patient to give up drink altogether.

* * *

In conclusion, although significant advances have been made in the therapy of delirium tremens, the number of deaths still appears to be unnecessarily high, particularly among cases complicated by infection or trauma. Obviously, treatment of complicating illness is of the utmost importance. Nevertheless, prompt control of delirium tremens itself is essential, since proper treatment of the complicating illness is generally impossible until the delirium is controlled or subsides. The mortality among the uncomplicated cases is low and, with regard to this group of patients, one can agree with the conclusion of Rosenbaum et al. that "the problem in delirium tremens at this time is not so much one of discovering the proper method of therapy as it is an elucidation of the etiologic factors involved."

295 Walnut Street
Brookline, Massachusetts

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THE WAR AND PUBLIC HEALTH

FREDERICK F. RUSSELL, M.D.*

BOSTON

THE military aspects of public health are many and varied. It is obvious that a healthy army and navy can be recruited only from a healthy population, and one may say without exaggeration that the public health of our nation furnishes the basis on which can be estimated the man power for the armed forces and for the war-production industries. During the present war it has often been wondered why the Italian troops were not better warriors and why their campaigns have not been more successful. Without knowing the reasons for the Italian failures, one may strongly suspect that the principal one has to do with public health in Italy. The Italian public health services have never been particularly distinguished in spite of the fact that a few eminent men have held posts in them. A large part of the population has for endless years been exposed to malaria, a particularly pernicious kind. Experience with this disease has demonstrated that chronic and repeated infections with malaria in endemic areas, such as southern and central Italy, produce a weakened population; not only is the health of the communities at a low level but also the economic condition of the people is depressed. Much of the southern Italian population is involved in a vicious cycle of disease, undernutrition, poor economic status, poor education and, worst of all, a low state of morale and a hopeless outlook for the future. With better public health in Italy the whole course of the Italian war efforts might have been quite different. There is nothing new about this idea, for the decadence of classical Greece has been almost

universally attributed to the invasion of the country by malaria at about the fifth century before Christ. The Greeks in their day could do nothing about this because no one had the necessary knowledge, but this is not true today. Malaria is now well understood, and if the Italians had used the available knowledge of the disease they could in all probability have controlled the greater part of it, just as has been done in this country.

Every activity of a state health department is important to the military services. Even the maternity and infant welfare divisions become fundamentally significant when we find it is obligatory to recruit eight or ten million young men and to enlist under a voluntary system large numbers of young women, and to continue these activities over an indefinite period of years. Everyone hopes that the duration of the war will be short, but the country must nevertheless prepare for a long war or run the risk of losing everything through inadequate preparation. If the states had had better divisions of maternity care and infant welfare during the last twenty years, it might not have been necessary to reject so many young people for disease of one sort or another during the present global war.

In the early days of conscription, before the Nation's actual entry into the war, the number of rejections at recruiting stations was, according to the reports of the selective service boards, about 500 men out of every 1000 examined. The majority of rejections were made because of disease or physical defects, but mental diseases of varying severity accounted for a considerable number. In the early

*Professor of preventive medicine, emeritus, Harvard Medical School

regimens. Scopolamine has been largely abandoned in routine therapy because of the uncertainty of its effect.

Vitamin and Dietary Therapy

Since the introduction of thiamine and nicotinic acid into general use, many reports have appeared purporting to show that they are curative in cases of delirium tremens. Suffice it to say that no report of dramatic success with these agents is convincing. Rapid cures in cases of delirium tremens treated with thiamine have been reported by Kiene et al.,²⁷ Cannon et al.,²⁸ who gave thiamine along with glucose and insulin, and Sciclounoff and Flagg.²⁹ It was Hammargren's³⁰ opinion that thiamine therapy in delirium tremens is sufficiently promising to warrant further investigation. Rosenbaum, Piker and Lederer,⁷ in controlled clinical observations on 36 cases of delirium tremens, found that the patients treated with thiamine required less paraldehyde than did the untreated groups. Nevertheless, they observed that two patients who had incipient delirium tremens on entry developed active delirium tremens after forty-eight hours in spite of large doses of thiamine. Jolliffe et al.^{31, 32} found that nicotinic acid produced dramatic cure in certain cases of alcoholic delirium that they distinguish from delirium tremens as "nicotinic acid deficiency encephalopathy." They point out, however, that in delirium tremens per se they do not consider thiamine or nicotinic acid deficiencies to be etiologically specific, nor do they consider these substances to be curative when used therapeutically. Thus one is forced to agree with Rosenbaum, Piker and Lederer⁷ that, once the disease starts, the addition of thiamine, nicotinic acid, liver extract and brewer's yeast does not aid in shortening the illness.

Nevertheless, to withhold generous quantities of vitamins from patients with delirium tremens appears to be shortsighted and academic. It is a matter of common experience that the patients are badly nourished and subject to gross avitaminoses. For this reason it seems desirable as suggested by Jolliffe et al.³² to correct faulty vitamin intakes in these patients, although dramatic curative results are not to be expected.

It is extremely important to restore patients who have had delirium tremens to adequate dietary intakes as soon as possible. In unco-operative patients, the administration of large quantities of semi-fluid food rich in carbohydrate and protein by stomach tube is of value. Such mixtures should preferably be divided into small amounts, to be given at frequent intervals.

Miscellaneous Measures

Few writers in recent years have failed to condemn the use of restraint in handling delirious patients, although some authorities recognize it as a necessary evil in situations in which nursing care

is limited. It should be emphasized that the experienced physician is apt to attempt to do a restraint what he has failed to achieve withatives and judicious handling of the patient.

Continuous tub baths for the afebrile or slightly febrile delirium tremens patient are recommended and are used in some clinics with excellent results. This type of therapy is rational and doubtless reduces considerably the amount of sedative medication needed in a given case, but it also requires facilities and man power than are available in an average public hospital.

Ideally, close attention should be paid to the surroundings in which a delirious patient is put. It is often bad practice to leave such patients in darkness, since this seems to increase the terrifying effect of hallucinations. Preferably lighting should be subdued but should extend to every corner of the room. Pictures on the wall are apt to provide the patient with further material for hallucinatory processes. Of extreme importance is the fact that the suicidal or homicidal tendencies of some delirious patients make the leaving of glassware and other loose objects in the room distinctly unwise.

Psychotherapy is of undoubted value in many cases of delirium tremens but is beyond the scope of this paper. In assaying the results of treatment which is often directed at actual cure of chronic alcoholism, it should not be forgotten that a single bout of full-blown "horrors" is sometimes followed by a prolonged period of abstinence, regardless of the therapy employed. In rare cases, a vigorous bout of delirium tremens may afford sufficient impetus to induce a patient to give up drink altogether.

* * *

In conclusion, although significant advances have been made in the therapy of delirium tremens, the number of deaths still appears to be unnecessarily high, particularly among cases complicated by infection or trauma. Obviously, treatment of complicating illness is of the utmost importance. Nevertheless, prompt control of delirium tremens itself is essential, since proper treatment of the complicating illness is generally impossible until the delirium is controlled or subsides. The mortality among the uncomplicated cases is low and, with regard to this group of patients, one can agree with the conclusion of Rosenbaum et al. that "the problem in delirium tremens at this time is not so much one of discovering the proper method of therapy as it is an elucidation of the etiologic factors involved."

295 Walnut Street
Brookline, Massachusetts

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THE WAR AND PUBLIC HEALTH

FREDERICK F. RUSSELL, M.D.*

BOSTON

THE military aspects of public health are many and varied. It is obvious that a healthy army and navy can be recruited only from a healthy population, and one may say without exaggeration that the public health of our nation furnishes the basis on which can be estimated the man power for the armed forces and for the war-production industries. During the present war it has often been wondered why the Italian troops were not better warriors and why their campaigns have not been more successful. Without knowing the reasons for the Italian failures, one may strongly suspect that the principal one has to do with public health in Italy. The Italian health services have never been particularly distinguished in spite of the fact that a few eminent men have held posts in them. A large part of the nation has for endless years been exposed to malaria of a particularly pernicious kind. Experience with the disease has demonstrated that chronic and repeated infections with malaria in endemic areas, such as southern and central Italy, produce a weakened population; not only is the health of the communities at a low level but also the economic condition of the people is depressed. Much of the southern Italian population is involved in a vicious circle of disease, undernutrition, poor economic status, poor education and, worst of all, a low state of morale and a hopeless outlook for the future. With better public health in Italy the whole course of the Italian war efforts might have been quite different. There is nothing new about this idea, for the decadence of classical Greece has been almost

universally attributed to the invasion of the country by malaria at about the fifth century before Christ. The Greeks in their day could do nothing about this because no one had the necessary knowledge, but this is not true today. Malaria is now well understood, and if the Italians had used the available knowledge of the disease they could in all probability have controlled the greater part of it, just as has been done in this country.

Every activity of a state health department is important to the military services. Even the maternity and infant welfare divisions become fundamentally significant when we find it is obligatory to recruit eight or ten million young men and to enlist under a voluntary system large numbers of young women, and to continue these activities over an indefinite period of years. Everyone hopes that the duration of the war will be short, but the country must nevertheless prepare for a long war or run the risk of losing everything through inadequate preparation. If the states had had better divisions of maternity care and infant welfare during the last twenty years, it might not have been necessary to reject so many young people for disease of one sort or another during the present global war.

In the early days of conscription, before the Nation's actual entry into the war, the number of rejections at recruiting stations was, according to the reports of the selective service boards, about 500 men out of every 1000 examined. The majority of rejections were made because of disease or physical defects, but mental diseases of varying severity accounted for a considerable number. In the early

*Professor of preventive medicine, emeritus, Harvard Medical School

days of the draft, about 35 men per 1000 were rejected for the latter reason, but later, when the Surgeon General had called special attention to the seriousness of abnormal mental states, the number of rejections increased to about 80 per 1000.

Another cause of rejection at the induction centers that shows an increasing rate is pulmonary tuberculosis. Although the plans of the Army and Navy called for physical examination, including x-ray examination of the chest, of all draftees, it was not possible in the early days of the war to obtain a sufficient number of x-ray machines to do the work. When, however, an adequate number of outfits became available, the rejection rate on account of pulmonary tuberculosis rose from 8 per 1000 in March, 1941, to 16 in January, 1942, and the rate continued to rise to 18 in September, 1942. This does not, of course, mean that the disease is increasing at this rate in the civil population, but merely that improved methods of diagnosis are giving a truer picture of the prevalence of pulmonary tuberculosis than has ever been obtained by the earlier methods. It also demonstrates quite clearly the need for universal x-ray examination of the chest in all properly conducted physical examinations, in civil life as well as in the armed forces.

Rejections because of cardiovascular disease, largely the results of rheumatic fever and of syphilis, amount to about 50 men per 1000. This high rate indicates clearly one of the important fields of study for the future. Cardiovascular disease due to syphilis is surely preventable and as such is of prime importance to all health authorities. In every war an increase in syphilis is to be expected; there will probably be an increase in this one, and the health authorities must make provision for it. Fairly good methods for the control of syphilis are available, and the Scandinavian countries, for example, have been highly successful in applying them. This country has lagged behind and is now faced with a problem of increasing size, so that it is important for health departments to overhaul their venereal-disease programs and make provision for extending and improving them.

Syphilis is a world-wide disease, but its virulence varies considerably in different parts of the world. It is well known that the syphilis of the Caribbean is mild, and it is for this reason that the theory of the American origin of syphilis has always struck me as sound. In the Orient, however, the disease is quite virulent. The syphilis in this country lies between the two extremes: that is, it is moderately severe. So far as is known, both the virulent and the mild forms respond well to the modern treatment that is now available.

Another venereal disease for which we must be on the lookout is lymphogranuloma venereum, which to most practitioners in this latitude is a new disease. It is of common occurrence in the tropics

and particularly so in the Caribbean area. Cases are not infrequent in Puerto Rico, Cuba and Central America. The disease has long been known as climatic bubo, and its venereal origin was for many years unrecognized. Now, however, it is known to be a virus disease acquired by sexual contact and is recognized as a serious public-health problem. It demands correct diagnosis, quarantine of the sort to prevent its spread and the best treatment possible. Unfortunately, up to the present there has been no known specific treatment, and one must do the best one can by expectant treatment. It has recently been determined that the infection, unlike most virus diseases, responds well to the sulfonamide drugs. If further experience shows that these drugs are curative, the task of eradication will be much simpler. Here is a field in which the health authorities should undertake some serious research. Why should they wait for other organizations or universities to solve the problems for them. Research in this field seems not merely a desirable activity but actually a fundamental duty of the health authorities. No one can foretell who will finally solve the problem, but the more investigators interest themselves in this relatively new venereal disease, the sooner will the problem be solved.

Health departments in the past have made notable progress in research, as witness the studies of Chapin, of Rhode Island, on measles; of Park on diphtheria; of the United States Public Health Service on endemic typhus fever, Rocky Mountain spotted fever and the effects of fluorine in the drinking water on mottled tooth enamel; and of the United States Army on yellow fever and typhoid fever. Both the Army and Navy have conducted extensive studies on the physiology of life at the high and low atmospheric pressures occurring in submarines and in the stratosphere. These are only a few examples of research by government bodies.

Cardiovascular disease due to rheumatic fever is still an epidemiologic puzzle, although much more is known about it than was the case during the last war. Many of the studies now being made of hemolytic streptococcus diseases are showing clearly the nature and extent of the problem. Furthermore, the recent experimental use of the sulfonamide drugs in the prophylaxis of streptococcal infections is extremely promising, and it is possible that in the future rheumatic fever and other streptococcal diseases will be much more successfully controlled than in the past. Already it is known that the routine administration of small doses of one or another of these drugs to all recruits during the first weeks of their service in the armed forces cuts down the amount of hemolytic streptococcus disease. As a method of control through the use of drugs, this experiment has been highly successful, but this does not mean that the method will ultimately prove to be either the best or the simplest one. The ad-

stration of any drug to hundreds or thousands of persons at frequent intervals over a period of weeks or months is extremely difficult and expensive, so that the search for some simpler means of control should not be relinquished. Drug control of disease has always been expensive both in money and in personnel. If the environment can be successfully dealt with, this will be easier than dealing with the patient. For this reason, studies are being made in many places to find, if possible, some promising method of control in this puzzling problem.

Micro-organisms in the air of hospital wards and churches, theaters and other places of public assembly can be controlled to a certain extent by the use of ultraviolet light, and also by some of the newer aerosols used as fine sprays.

Vaccination or immunization as a method of control of streptococcal infections has not as yet been successful, perhaps because a mixed group of infections is concerned rather than a single well-standardized disease. Yet one is not justified in giving up the possibility, and research will of course be continued on the subject of immunization as a method of control of the streptococcal infections.

The subject of social medicine after the war deserves consideration. The plans of the Army and Navy for the care of returned soldiers and sailors are elaborate, and since the number of persons to be in care of is extremely large, — already almost 10,000 have been returned to civil life for one reason or another, — it is apparent that this example of social medicine is bound to have a considerable effect on future health policies. Just what will follow is not clear at the time, but it does not seem improbable that a greater interest in all the aspects of social medicine will be aroused. Following the war, the government developed an extensive system of veterans' hospitals, but they have had little direct effect on the practice of medicine. On the other hand, a new and quite successful development in medical care has occurred since the last war; namely, the hospital insurance systems that have sprung up all over the country. The Blue Cross organization for hospital insurance in Massachusetts seems to have been highly successful, and the use of the system on a voluntary basis is increasing. The medical profession and the public have accepted this program quite generally, and it has helped both the patients and the hospitals. The question is now whether the Blue Shield, a sickness insurance on similar lines, will be equally successful.

A good deal has been said about the introduction of exotic diseases by returning soldiers, and the principal disease referred to is malaria. It is unfortunately true that there is much endemic malaria in the several war zones. In North Africa, for example, there is widespread endemic malaria among the native populations, the malarial season is long, and transmission to the American troops is in-

evitable. It will be recalled that in 1880 Laveran discovered the plasmodium of malaria while working with French troops in Algeria. Unfortunately, the disease is still extremely prevalent there, even though sixty years have passed since Laveran made his discovery. From North Africa the troops went to Sicily, and there again were exposed to a population that has suffered from widespread endemic malaria for hundreds of years. When they crossed over the Straits of Messina to invade Calabria and southern Italy the situation was not changed, for malaria is endemic all over southern and middle Italy. It is only during the last ten years that some control has been obtained over the malaria in the Pontine Marshes and the surroundings of Rome.

The endemic malaria of the Mediterranean is not limited to Italy but is equally prevalent east of the Adriatic in Greece, Albania and southern Yugoslavia. Everyone knows of the almost epidemic prevalence of malaria in the islands of the South Seas, particularly in the Solomon Islands. The troops occupying those islands must be replaced at frequent intervals by healthy ones, and the returning troops must be put into rest areas with good hospital facilities, since almost every man in each division will need treatment and care for a time.

Malaria is not an acute disease in the ordinary sense of the word. It is really a relapsing disease that may continue to manifest itself for a year or two after the first attack. It is no longer considered necessary to discharge a man from the service because of malaria, for he can be treated and will recover from the infection just as well while in the service as at home. There are, however, many wounded men and sufferers from some chronic disease, mental or physical, who have malaria in addition to their principal disease, and these men will be sent home for proper treatment and ultimate discharge, when they will play the role of more or less chronic malarial carriers. These are bound to be a considerable element in the population of the Army hospitals at Framingham and Fort Devens. The question to be asked is, How much of a problem do they present to the public health of the adjoining communities? Undoubtedly there will be a considerable number of malaria carriers in the hospitals of this state. Since the disease is never passed along to new victims by contact, but only by the bite of *Anopheles quadrimaculatus*, the anopheline of this region, the number of secondary cases will depend directly on the number of these mosquitoes in the neighborhood of the hospitals. The Army authorities can be counted on to suppress all breeding of anophelines on the military reservations, but this will not be enough to protect the adjoining communities if they have extensive breeding areas. It is therefore obvious that these communities should make a survey of the anopheline population in their townships, so that they may make tentative plans for mosquito control later, provided that it becomes

necessary. Theoretically, it is possible to have extensive malaria in this state, but there is another side to the question. The mosquito breeding season at this latitude is short — probably less than three months each year. The number of anopheline breeding places is probably not very large anywhere in the Commonwealth. Malaria carriers have been coming here from the tropics, from our own South and from Greece and Italy over a period of many years, and the number of secondary cases of malaria that have resulted has been extremely small. There has never been falciparum or tropical malaria or quartan malaria in this region, and the only form that must be planned for is vivax or tertian malaria, which is the mildest of all the forms of the disease, with a low death rate. One must not, however, be too complaisant about the situation, since no one has any idea as to the number of carriers that will be sent here, or just how prolific the anopheline breeding will be in any particular year. All cases of malaria must be reported, and the means of anopheline control must be in readiness in the neighborhood of every Army and Navy hospital.

Some of the malarial relapses will come after the men have been discharged from the armed services and are in their homes. In this situation, the disease must be diagnosed and treated by the local practitioner. He will have the help of the state public-health laboratory and the advice of the district health office, in addition to that of the local health department. This aspect of malaria in Massachusetts should not be a serious one, since the majority of physicians and public-health officers are well trained, the means of communication are unsurpassed, and any local outbreak can be quickly controlled. Such control has not always been easy, however, and in Russia following the last war there was a terrific epidemic of malaria that extended to Archangel, above the Arctic Circle. Much the same kind of catastrophe occurred in the Balkans, and malaria was epidemic there for many years after the war. In both these regions the devastation from the war was colossal and the ways of living were primitive, and it took many years to gain the upper hand over malaria and typhus fever. Conditions in Massachusetts are so different that no such epidemic need be feared. Mosquito and fly screens are in general use, and malaria patients can and should be housed in screened buildings. Adult mosquitoes should be killed by sprays as rapidly as they are discovered. There are enough physicians to make the diagnosis and give the proper treatment, and enough health officers to identify and control the anopheline breeding in every threatened locality.

One fact worth emphasizing is that malaria has never been controlled by the administration of quinine or any other drug to its victims. It has always been necessary to control anopheline breeding to gain the upper hand of malaria transmission,

and in the end this form of control is not only more satisfactory but also much cheaper than the treatment of patients.

Typhus fever is another exotic disease that may cause a great amount of difficulty in North Africa, in Italy and more especially in the Balkans, but it is a louse-borne disease and need not be feared in this state, for since the Civil War we have not been a lousy people. The disease may be introduced by returning troops or by refugees from eastern Europe, but it will not spread. Had the eastern coast of the United States been invaded by the Germans and had the cities been subjected to destruction, the usual protection against lice would have been lacking, but as things are today there is no danger of this. In the area of operations typhus fever among the troops is almost unknown, in spite of the fact that something like 75,000 cases have been reported in the North African native population. Freedom from this infectious disease is owed to two things: an efficient vaccine and a repellent powder that is dusted into the underclothes of each man and promptly kills not only the adult lice but also the nits in the seams of the clothes. The effect of one dose of the powder lasts for several days, and it is easily and inexpensively renewed.

With many prophylactic procedures, such as small-pox vaccination, it is sometimes difficult to secure the co-operation of the public, but in this anti-louse, anti-typhus fever campaign, the natives welcome the new treatment, and in some places they have made themselves more or less of a nuisance by demanding frequent and repeated delousing. One wonders whether the North African, as a result of the prophylactic methods of the health departments of the military and civil governments, may not turn out to be a much more acceptable citizen of the world than he has been in the past. Who knows how far he may advance in his civilization if once he is freed from the diseases that have for so long interfered with his cultural and economic development?

To return for a moment to the personnel of the public-health and medical services: men have been sent from civil life into the armed forces, and, in addition, a large number of recent medical-school graduates have been taken who would ordinarily have gone into practice at home. The total number of doctors involved may be estimated at 50,000. What sort of experience will this large group have in the armed services? To be sure, medicine and public health are the same in principle in peace as in war, but care of the civilian population is different from that of the soldier or sailor. For example, the medical officer does not, as a rule, deal at all with chronic disease or the problems of the aged. The Army or Navy doctor deals chiefly with acute disease, and his prime object is to take care of the lesser diseases and injuries so that his patients may return to the firing line as soon as possible. The

vention and treatment of diseases and of injuries that frequently result in chronic disability, such as tuberculosis, are of course important but for the military man they are less important than the proper treatment of self-limited diseases and for injuries. The physician in civil life spends much more of his time and energy in the care of chronic and more or less disabling diseases, and thus it is seen that there is a wide divergence in the point of view of the military and the civil surgeon.

Medicine in the Army, just as in civil life, includes the specialties, and one of these specialties is preventive medicine. It is safe to say that the percentage of doctors in the armed services who act as health officers is much higher than it is in civil life. Every division and army corps and army has its own health officers and its health-department laboratory and statistical department, and in all commands the senior surgeon is also the health officer. When these men return home to civil life there will be a considerable number who have been active in preventive medicine and health-department activities. Some will then go into health departments, but even if they go into general practice they will understand and be sympathetic with health-department activities.

The health departments have lost many of their members to the Army and Navy, and one wonders whether either they or the public will be satisfied if the old health departments are restored to their former strength and activities. It is impossible to know, but it seems probable that there will have to be better health officials and larger health departments after the war. The medical men and the public have seen or learned of the great advances that have been made during the war in the prevention of disease. They both know that much more can be accomplished in the detection and prevention of tuberculosis, for example, than has been done in the past, and so with many other diseases, such as the venereal diseases. There is no doubt that the public will be willing to pay for the increased activities of the health departments, and thus the physicians of the country will join. Paradoxical as it may seem, it is true that a physician can make a better living in a prosperous, healthy community than he can in a population continually made poor by endemic disease, whatever its nature.

Parasitology promises to be a subject of importance in the post-war world. In this state there are many intestinal parasites — a few round worms, tapeworms and an occasional tapeworm. Returning troops, however, will bring back others. The flies should be examined for parasites, and the sinophilia that goes with many infestations should not be overlooked. The extensive spread of para-

sitic disease need not be feared, since the winters are long and cold and sanitation is good. Nevertheless, the infected patient must have proper treatment.

The importance of psychiatry in post-war medicine and public health is already apparent. The morale of the returned soldier must be kept up, and he must be assisted in finding his niche in a peaceful world. What can be done to prevent the development of neuroses and psychoses is a problem worthy of further study by health departments — national, state and local.

Does the present condition of public health at home and abroad suggest any modification of our own state and local health programs? It is quite true that this state has shown good leadership in the past, and that it has, in general, good laws and flexible regulations, and it is also true that the scientific background on which public-health laws and regulations are based has been conspicuously good.

The administrative side of public health has an interesting history. As times changed and new knowledge became available, the Commonwealth has changed its form of organization, and almost every year has seen some advance in methods of bringing health to the public. Development of state and local health departments is a process that is never finished. What are the present weak points in our organization and what are the changes that should next be made? Health departments based on the small-town system of government are weak and ineffective, and they need constant help from the state health department. One cause of their difficulty is that the board of health is an executive rather than a consultative body and, as is well known, administration by a board rather than by a full-time medical officer of health is necessarily slow and cumbersome. A more modern form of organization is a full-time health officer who has an advisory council, rather than an administrative board of health. The Worcester County board has recently been reorganized on this plan, and the new body may furnish a model for future reorganizations.

Massachusetts has in the past reorganized its public-health system to meet current needs, and it will of course bring its organization into conformity with modern practice. The present is an appropriate time to make plans for the future, since health departments will be more important to the people of all states than they have been in the recent past. Massachusetts has an opportunity again to show its capacity for leadership in public health and its ability to set a model for New England.

25 Shattuck Street

ECHINOCOCCAL DISEASE

A Report of Two Cases

THACHER W. WORTHEN, M.D.,* AND JOSEPH F. JENOVESE, M.D.†

HARTFORD, CONNECTICUT

ECHINOCOCCAL disease is most prevalent in the sheep-raising and cattle-raising districts of South America, Australia, South Africa, Central and Northern Europe and the Mediterranean countries of Asia and Africa. In North America 482 cases of hydatid disease in man have been reported since 1808, and of these 22 were indigenous. It is important to bear in mind that a large proportion of the immigrant population of the northern coastal states has come from countries where the disease is most frequently found. It should therefore be considered as a diagnostic possibility when atypical symptoms appear in a patient who has previously lived in one of these countries.

The disease is transmitted from sheep or cattle to dogs, which act as the intermediary host. The human infection results from contact with infected dogs. The ova may be present in the oral secretions or on the fur of the animal. The infection in man manifests itself in the form of cysts, which are either of the unilocular type or contain multiple daughter and even granddaughter cysts.

About 75 per cent of cases of echinococcal disease are found in the liver. Over three quarters of the cysts in the liver are located on the inferior surface of the right lobe so that they extend down into the abdominal cavity. The second most frequent site is the lungs.

In the clinical records of the Hartford Hospital covering a period of seventeen years, 7 cases of hydatid disease were found. Of these, 5 were echinococcal disease of the liver, 1 of the lung and 1 of the gluteal region. Four of the cases showing liver involvement had a cyst on the inferior surface of the right lobe.

This paper is primarily concerned with echinococcal disease of the liver, the symptoms of which may be simply those of a slow-growing tumor, which in time becomes palpable and causes pressure on the biliary tract and in rare cases ruptures.

Echinococcal disease of the liver may be difficult to diagnose because the symptoms may simulate involvement of the biliary tract. The following case report will serve to illustrate this diagnostic problem.

CASE 1. The patient, R. L., was a 41-year-old man who was born in Sicily, where he lived for 27 years. His trade was that of a bricklayer, but he was also employed as a policeman. In the latter capacity he was delegated to watch herds of sheep, and thus the canine contact was established. When he was 27 years old he immigrated to New York City, remaining there only 2 or 3 weeks prior to coming to Hartford, where he had lived since that time.

The patient was first seen by one of us (T. W. W.) in 1932 at which time he gave a history of having had discomfort in the right upper quadrant of the abdomen for approximately 8 years. This discomfort was in the form of typical colicky bladder attacks, pain being referred to the back, associated with vomiting and with dark-colored urine, although jaundice was actually described by the patient. A cholecystogram taken in 1932 revealed a gall bladder with somewhat reduced function but reasonably well outlined. An operation performed purely on the basis of the clinical history revealed slight thickening of the wall of the gall bladder, but no stone. There was an enlarged node along the cystic duct. The liver was perfectly normal in appearance and there was no fibrosis along its edge. No adhesions were present. Cholecystectomy was performed, with an uneventful convalescence.

For some 2 or 3 months after the operation there was relief of the symptoms, but the episodes of distress in the right upper quadrant then began to recur. During the ensuing decade there were from two to five attacks each year.

In March, 1942, the patient was seen by one of us (J. F.). From the past history and symptoms a stone in the common duct was suspected, although there was no jaundice and no bile in the urine. Dietary suggestions were made, and the patient was advised to report when another episode occurred. He was not seen again until 1 year later. At that time he presented the symptoms of an acutely ill patient. The sclerae showed jaundice and the urine contained bile. He stated that he had had a great deal of distress in the right upper quadrant, nausea and vomiting for several days. The stools were clay colored, and there was a positive direct van den Bergh reaction, the bilirubin level being 5.9 mg. per 100 cc. A smooth liver edge was palpable below the costal margin. It was suspected that a stone in the common duct was the basis of the trouble.

An exploratory laparotomy was advised and performed by one of us (T. W. W.). A few intra-abdominal adhesions were encountered. There was an irregular nodular mass just medial to the gall-bladder bed on the inferior surface of the right lobe of the liver. This mass extended from the superior to the inferior border of the liver, and the lower portion of it seemed to involve the hepatic ducts. Its appearance suggested a metastatic lesion, most likely secondary to a primary tumor in the biliary ducts. A biopsy was taken, and in the process a single drop of slightly cloudy fluid escaped.

The patient made an uneventful recovery, and the jaundice and bilirubin cleared up within 1 week. He has returned to work and is in excellent condition, having had no attacks since the operation 8 months ago.

Pathologic examination of the biopsy specimen revealed a chronic granulomatous process with a central mass containing hooklets typical of an echinococcal infection. Subsequent to this report a blood smear was obtained that showed 8 per cent eosinophils.

It is probably true that this patient acquired his infection in Sicily some eighteen years before the diagnosis was made. It would be difficult to believe that there was no visible evidence of echinococcal infection in the liver at the first operation if the operative notes were not so complete.

The only plausible explanations seem to be either that the lesion was beneath the surface of the liver at the time of the first operation or that a small lesion was overlooked, that a very slow growth ensued and that intermittent attacks of mild cholangitis accounted for the symptoms. Finally, a severe acute cholangitis indicated further surgery. In

*Visiting surgeon, Hartford Hospital.

†Assistant physician, Hartford Hospital (on leave of absence)

spect the long duration of the illness was definitely against a stone in the common duct, but nevertheless this was considered the most likely diagnosis. The complete relief of symptoms following the second operation is extremely interesting. This has been purely a coincidence — the cholangitis would have subsided of its own accord. Certainly there was no evidence of a stone in the common duct that manipulation might have dislodged. In any case it is rather too much to expect that this patient will have no further symptoms except for the fact that the natural course of the disease in many cases seems to be a favorable one. It is well to bear this statement in mind as one considers the course of the second case, which presented no obvious diagnostic problem.

CASE 2. M. G., a 34-year-old man born in this country, admitted to the Hartford Hospital in February, 1935, with a mass 6 cm. in diameter in the midepigastrium that had been present for years. Radiologic investigation revealed that the mass was anterior to the stomach. The patient was jaundiced. There was an eosinophilia of 25 per cent. At operation a cyst the size of a large grapefruit was found partially incorporated in the liver substance. The liver itself was riddled with innumerable cysts varying in size from that of the head of a pin to that of a small marble. The contents of the large cyst were completely evacuated, a great many smaller cysts being found, and marsupialization was carried out. The immediate postoperative course was exceedingly uneventful. The patient had a toxic hepatitis and was on the critical list for 8 days. He was finally discharged, however, five weeks after operation with a profusely draining sinus. The

eosinophils had dropped to 2 per cent and have been normal ever since. He returned to work about a year later with a persistent draining sinus that necessitated daily passage of a small catheter to prevent obstruction.

This process continued for the ensuing $7\frac{1}{2}$ years, during which time periodic returns to the hospital were required for the dilatation of the stricture of the sinus, which recurred in spite of the dilatation by catheter.

The sinus has now been closed for 10 months, the liver is not palpable, and the patient is apparently well.

SUMMARY AND CONCLUSIONS

Two cases of echinococcal cyst of the liver have been reported, one of long duration (eighteen years) with symptoms much akin to those of disease of the biliary tract, the diagnosis being made by biopsy at the second operation.

The second case, also of many years' duration, was diagnosed, came to operation, and was finally followed by the spontaneous closure of a sinus resulting from marsupialization. The fact that this patient was a native-born American is unusual but not unknown. It merely serves to emphasize that one cannot make a diagnosis of echinococcal disease purely on the basis of nativity.

The consciousness of the possibility of the occurrence of echinococcal disease of the liver may lead to a diagnosis of this condition in certain cases of atypical biliary-tract disease.

179 Allyn Street

MEDICAL PROGRESS

RECENT ADVANCES IN SURGERY*

ALFRED BLALOCK, M.D.†

BALTIMORE

THE golden age of surgery is said to be that which followed the introduction of methods for producing surgical anesthesia and for lessening the incidence of infections. These and other discoveries widened the scope of surgery to an amazing degree. Undue haste in the performance of operations was no longer necessary. The type of alteration that occurred is illustrated by a quotation from Cushing.¹

The accurate and detailed methods, in the use of which Kocher and Halsted were for so long the notable examples, have spread into all clinics — at least into those clinics where you or I would wish to entrust ourselves for operation. Observers no longer expect to be thrilled in an operating room; the spectacular public performances of the past, no longer condoned, are replaced by the quiet, rather tedious procedures which few beyond the operator, his assistants and the immediate bystander can profitably see. The patient on the table, like the passenger in a car, runs greater risks if he have a loquacious driver, or one who takes close corners, exceeds the speed limit or rides to applause.

*From the Department of Surgery, Johns Hopkins University and Hospital.

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Surgeon-in-chief, Johns Hopkins Hospital, professor of surgery, Johns Hopkins University School of Medicine.

The latter part of the last century is perhaps best known for advances in the surgery of the intestinal tract, of the breast, of hernia, of the thyroid gland and of the pelvic organs. The second and third decades of the present century are perhaps most notable for the advances in neurosurgery, whereas thoracic surgery made great strides in the fourth decade. This division is of course an artificial one, since there has been a steady progress in all phases of surgery. When considered from month to month these advances do not seem very great, but when viewed after a lapse of several years the progress is striking. Many examples could be given that would illustrate the remarkable increase in the number of fields in which surgical therapy is being employed. According to Alexander,² only about 300 cases of pulmonary tuberculosis were reported as having been operated on in the United States between the years 1918 and 1925. It is true that in this particular development we followed at a slow pace the lead of surgeons in other countries. Operations on the heart, the esophagus, the diaphragm,

the lungs, the spinal column, the pancreas, the blood vessels and other structures have increased greatly in number in recent years. It is of interest to consider some of the causes for this increase.

In the first place, a larger number of operations are being performed because of earlier and more accurate diagnosis. This fact is due not so much to improvements in methods of history taking and physical examination, which have advanced very little in recent years, as to advances in other diagnostic methods. Notable among these is the more frequent use of the roentgen ray, together with the employment of various contrast mediums. It would be impossible today to practice surgery effectively without the benefit of the knowledge gained from the gastrointestinal series, the barium enema, cholecystography, pyelography, ventriculography, bronchography and arteriography. What satisfaction must attend Dr. Cannon, Dr. Graham, Dr. Dandy and others who have been responsible for advances that have resulted in the earlier and the more accurate diagnosis of various diseases! A number of years ago most operations were listed as exploratory procedures. This meant that one was usually in doubt where to make the incision, was frequently unable to locate the diseased area at the time of operation if changes were minimal and usually had to cause a good deal of trauma to normal parts in order to locate the site of the disease. A striking example of the value of the roentgen ray is shown in the recognition of diaphragmatic hernias. In 1938 Harrington³ stated that the condition was recognized at the Mayo Clinic in more than twenty-three times as many cases in the last twelve years as in the previous eighteen years.

Surgery must prove itself continually in that the benefits to be derived from an operation must outweigh the risk to life, the discomforts, the loss of time and the expense. Earlier diagnosis has been an important element in reducing the morbidity and mortality rates associated with operations. This in turn has given patients an increased confidence in what can be accomplished by surgical means, and there is less tendency on the part of the public to conceal trouble until far-advanced disease is present. The intelligent use of the roentgen ray has played a major part in this transformation. It appears to be a safe prediction that, in the future, roentgenographic studies of the chest will be made routinely on all patients. Already many asymptomatic disorders of the chest have been discovered during examination of recruits for military duty. It is just as important that the surgeon should have the advantage of the opinion of a good roentgenologist as that he should have the advice and counsel of a good internist.

Advances in the knowledge of the causes of disease also have widened the scope of surgery. Operations on the parathyroid and adrenal glands and the pancreas have ceased to be of rare occurrence.

A better understanding of the functions of the sympathetic nervous system and its relation to various diseases has multiplied many times the number of operations on this system. Similar statements might be made about various other parts of the body.

Advances in the preoperative and postoperative care of patients have played a large part in the progress of surgery. Rarely today are emergency operations performed on moribund patients, since most cases means are available for improving the condition. Hemorrhage that is uncontrollable by nonoperative means is one of the few indications for immediate operation. One is seldom justified in operating before dehydration or acidosis and other such conditions have been corrected. Fortunately, the patient consults the physician earlier today than previously, and the difficulties connected with the preparation of the patient are relatively fewer. The incidence of preoperative complications has diminished considerably, and means are available for dealing effectively with a good many of those that do occur.

Measures that are helpful in preventing pulmonary embolism deserve special emphasis. These include an appreciation of the value of frequent alteration of the position of the patient, of the use of heparin and dicumarol and of ligation of the femoral vein when indicated. Notable among the recent achievements are the various chemotherapeutic agents for preventing and combating infection and the several different methods by which intestinal distention due to a number of causes can be relieved. Great credit is due Drs. Collier and Maddock for their important studies on fluid balance in surgical patients. The problem of the feeding of patients by the intravenous route is only partly solved, but even so the results are significant and encouraging. Some of these advances will be commented on later. Lord Moynihan has said that surgery has been made safe for the patient and that we must now make the patient safe for surgery. Important strides have been made in this direction but it is likely that the next several decades will see greater progress.

It is difficult to assess the advances in anesthesia from year to year, but the progress from decade to decade is fully evident. There are improvements in methods of administration as well as a larger number of satisfactory agents from which one may choose. There are now many anesthetists and surgeons who can choose in an intelligent manner the best anesthetic agent for the patient in question. The reduction of untoward incidents both during and following operation is due in no small measure to such advances.

There is probably no measure that has contributed more to the manner in which operative procedures of great magnitude are withstood by patients than the copious use of blood and blood

titutes. It appears to be generally agreed that does not wait for the appearance of fully developed shock before instituting therapy. One should prevent or treat shock according to the severity of the duration of the operative procedure, the degree of blood loss and the previous condition of the patient rather than wait for an alteration in the concentration of the red corpuscles or for a severe fall in blood pressure. Traumatic shock may develop without any significant alteration in the rate of the pulse or in the concentration of red corpuscles. A decline in the arterial pressure to 60 mm. of mercury is frequently a sign of advanced rather than of early shock. At the beginning of all operative procedures of considerable magnitude a needle should be placed in an accessible vein and fluid should be administered as indicated. The quantity of blood or blood substitute required varies from patient to patient. As Dr. Harkins has said, there is no more logic in giving the same quantity of blood to every surgical patient than there would be in prescribing the same dose of insulin for every patient with diabetes. At any rate, attempts to maintain the blood volume at essentially the normal range during operative procedures have resulted in a widening of the scope of surgery, fewer deaths at the time of operation and a reduction in postoperative complications.

The importance of replacing protein that may be lost in various surgical conditions has received much attention in recent years. Protein deficiencies may be responsible, at least in part, for a number of complications, including wound disruption, abdominal distention, edema, anuria and circulatory failure. The intravenous injection of blood plasma is an efficient method for correcting acute hypoproteinemia, but it is a rather expensive and time-consuming method for giving protein nourishment. With this in mind, Elman⁴ gave a high-protein diet by mouth, but since vomiting frequently rendered this method ineffective he resorted to the use of hydrolyzed protein by intravenous injection. Subsequent work has shown that the principle of introducing the building stores of protein — amino acids and peptides — is sound. This method is now used clinically rather extensively. Although some untoward reactions have been reported and although there are some contraindications to the giving of amino acids intravenously, the results are in general extremely encouraging. Protein deficiencies can be corrected and, more important, they may be prevented by the early administration of an appropriate mixture of amino acids in cases in which adequate amounts of protein cannot be taken by mouth or cannot be assimilated when so taken. This physiologic short cut in protein nutrition, with the addition of water, electrolytes, glucose and vitamins, provides an almost complete intravenous diet. The advantages of the preoperative correction and the postoperative prevention of nutritional disturbances

are obvious; patients can be more adequately prepared for operation and the morbidity and mortality rates can be reduced.

Advances in chemotherapy have had a far-reaching effect on surgery. One cannot help being impressed by the radically altered outlook for patients with septicemia, meningitis, peritonitis and pneumonia that has been effected through the use of sulfonamides and, even more strikingly, that of penicillin. It is difficult in some cases to differentiate the role of chemotherapy and that of transfusions in bringing about this altered picture, because both have played their respective parts, as have better methods of maintaining balance of fluids and electrolytes and nutrition. Now that penicillin has demonstrated its ability to deal with invasive staphylococcal infections, and in view of the promise of still newer antibiotic agents in dealing with infections due to gram-negative bacilli, it seems that in a few years it will be necessary much less often to record a death as having been due to bacterial infection. Such an optimistic statement should probably be followed by an admission of our inability at present to treat effectively by chemotherapy such disorders as chronic ulcerative colitis, regional ileitis, tuberculosis, thromboangiitis obliterans and certain mixed infections of the lung and peritoneum.

Advances in chemotherapy have in no sense lessened the importance of familiarity with and careful observation of certain general practices, such as careful hemostasis and the gentle handling of tissues. It has been shown that infection will develop in wounds even in the presence of potent antibacterial drugs if there exists an unfavorable adjustment of factors concerned in repair. This observation is both an expression of the limitations of the drugs and a warning to the surgeon to observe well-established principles if he wishes to avoid infection. Tissues usually tolerate a moderate degree of contamination if the mechanisms of local resistance are not disrupted by unnecessary damage. The use of agents that suppress bacterial growth has made more evident the importance of a good surgical technic.

If one is to treat the so-called "surgical infections" intelligently, one must differentiate the systemic and local components. The local component is usually characterized at some time in its course by necrosis of tissue. Because integrity of the blood supply is essential for the systemic distribution of the drug to the site of infection, the greatest effectiveness of the agents is observed in treating the invasive types or stages of infection. Under such circumstances the necessity for treatment by operative means may be obviated, but it must be emphasized that the local accumulation of pus should be treated by open drainage. It appears that the use of chemotherapeutic agents has increased the number of cases in which local drainage

only is employed because of the striking reduction in the mortality rate associated with the systemic component of the infection. Thus far, the results that have followed the local use of the various chemotherapeutic agents in the treatment of infected wounds of soft parts and of chronically infected ulcers have not been encouraging.

The problem of operating-room infections continues to be a real one, particularly during the periods when there are many diseases of the respiratory tract. Thanks to the various chemotherapeutic agents, such infections rarely cause death, but they may cause wound disruption and other complications. The work of Hart⁵ and others on the sterilization of air by bactericidal radiation has yielded encouraging results. Perhaps even more practical will be the use of glycol vapors as developed by Robertson⁶ and his associates. Further progress in this important field is awaited with interest.

* * *

The next topic is a consideration of some of the advances in surgery that apply to a particular organ or structure. These will be discussed in a general way, and it is hoped that failure to refer to much important work will be pardoned.

THE ESOPHAGUS

There are few parts of the body — and certainly no part of the intestinal tract — that have presented as many impediments to progress in surgery as has the esophagus. This appears to be mainly due to the fact that the blood supply of the esophagus is relatively poor, that this organ has no serosal covering and that unlike most of the intestinal tract it is a straight tube without a mesentery and without redundancy. Furthermore, it is relatively inaccessible, and the body tolerates infections of the mediastinum extremely poorly.

Carcinoma

A variety of factors in addition to those enumerated above have contributed to delay in advancement in the treatment of carcinoma of the esophagus. The onset may be insidious, and direct extension of the growth or distant metastases may be present before the symptoms cause the patient to consult a physician. The physician himself may not pay sufficient attention to complaints of slight dysphagia or moderate loss of weight. The advanced age of many of these patients has also been a handicap.

Torek⁷ performed a successful resection — without anastomosis — of the midthoracic esophagus for carcinoma in 1913. The patient died of pneumonia thirteen years later. Between 1913 and 1938 a total of thirty-four successful resections of the esophagus for carcinoma were reported by eighteen authors. It is doubtful whether any of these patients lived as

long as five years. The largest series of cases reported by Ohsawa⁸ in 1934. According to Adair^{9, 10} Ohsawa reported four successful resections in cases of carcinoma of the thoracic esophagus, eight successful resections in 14 cases of carcinoma involving the cardia and esophagus, in which 2 to 10 cm. of the esophagus was resected, one successful resection in 5 cases in which 6 to 8 cm. was removed, and two successful operations in which an esophageal jejunostomy was performed.

Since 1938 much attention has been directed to the treatment of carcinoma of the esophagus, and many successful operations have been performed. Except for the problems that are common to the surgery of cancer in general, — namely, those of direct extension and metastasis, — it may be stated that surgery of the lower fourth of the esophagus and cardia has progressed¹¹ in a highly gratifying manner. In other words, satisfactory means are available for removing the lower part of the esophagus and cardia, for mobilizing the stomach and for making an intrathoracic anastomosis of the stomach and the esophagus. To what is this progress due? An occasional advance in surgery can be attributed to a single important discovery, but most of the advances are due to a number of more or less independent observations. Recent progress in surgery of the esophagus fits into this category. Among the many factors that have contributed have been earlier diagnosis as a result of the use of the barium meal and the esophagoscope, better preoperative and postoperative treatment, the more frequent use of transfusions and improvements in technical procedures. The latter include operative details such as the mobilization of the upper end of the stomach, the making of the new anastomosis at a point other than the previous opening and the anchoring of the stomach in the lower part of the chest in order to avoid tension on the suture line of the anastomosis. The experimental observations of Adams and Phemister¹⁰ and of Carter¹² have been particularly helpful in clarifying these points.

Operations on the upper three fourths of the esophagus have been less satisfactory, mainly because of the difficulty in re-establishing the continuity of the alimentary tract. The upper fourth, that part between the base of the neck and the superior surface of the aortic arch, presents an added difficulty in that the proximal esophageal end is so short that the establishment of an external fistula may not be possible. Garlock¹³ has recently reported the result in a patient with carcinoma of the midportion of the esophagus in whom he was able to mobilize the stomach sufficiently to make the anastomosis at a level just below the aortic arch. If one is able to remove the growth and to bring out the upper end of the esophagus, the possibility of connecting this to the stomach by a tube of skin or of rubber always remains, but it is not a desirable type of anastomosis.

ing the last two years Rienhoff¹⁴ has used a variation of the method of Roux¹⁵ in the treatment of carcinoma of the esophagus. The large vessels leading to a segment of jejunum are divided, the superior mesenteric artery, the jejunum is brought across at one point, and the mobilized end is brought through the diaphragm and the chest rather than through a tunnel beneath the skin of the chest wall. In this manner it is possible to obtain enough viable jejunum for replacement of the resected esophagus. Sweet¹⁶ has recently described a modification of the Roux procedure that aids in the mobilization of an undivided segment of the jejunum. This method can be used when the defect that is to be bridged is not so great as that mentioned above.

Esophageal Strictures

Most patients in whom strictures of the esophagus develop as a result of the swallowing of chemicals can be carried along fairly satisfactorily by repeated dilatations. There are some, however, in whom the obstruction becomes complete. One of the main difficulties in esophageal reconstruction from whole intestine is the appearance of fistulas at the point of anastomosis of the skin with the esophagus or the stomach, particularly the latter. Additional disadvantages are the multiple operative procedures that are necessary in order to complete the tube of skin and the absence of peristalsis. Other measures that have been used in the making of an artificial esophagus include the placing beneath the skin of the anterior chest wall of a mobilized loop of the colon, the greater part of the mobilized stomach or a gastric tube that is constructed from the greater curvature of the stomach. The various methods are reviewed in an excellent article by Ochsner and Owens.¹⁷ Yurasov¹⁸ has stated recently:

The brilliant idea formulated by Roux and Gerzen of substituting a mobilized segment of the jejunum for the original, useless esophagus was first put into practice by Gerzen in 1908, but found few adherents because of the high incidence of necrosis in the mobilized jejunal loop. Slight changes in this technique introduced by Lexer in 1911 to a very large degree obviated this danger.

Lexer¹⁹ brought the jejunal loop up to the mid-portion of the anterior wall of the chest and employed a short tube of skin leading to the cervical esophagus. This technic has been until recently the procedure of choice in the creation of any artificial esophagus. Because of the multiple stages necessary, because of ulcers at the junction of skin and mucous membrane and because of the absence of peristaltic movement in the skin tube, Yudin has abandoned the Lexer technic and has modified slightly the original Roux procedure.

The technic of Yudin²⁰ has not been described in detail; but it is essentially the Roux procedure. A section of jejunum 30 to 40 cm. in length is mobilized by dividing the vascular pedicle near the root of the mesentery. At a second stage the jejunum is divided proximally and the end of the mobilized

section is placed in a tunnel beneath the skin of the anterior chest wall that extends to the mandible. At this or a subsequent operation the jejunum is anastomosed to the side of the esophagus at a level just above the clavicle. Regarding the results Yurasov,¹⁸ Yudin's associate, stated: "We have performed thirty-eight esophagoplasties by bringing the jejunum up to the clavicle. In 14 of these cases the cervical segment of the esophagus was anastomosed with the jejunum. . . . We lost only 4 of our 38 patients."

Yudin's success may be explained in part by the fact that he was dealing with a benign lesion and that it was not necessary to divide the esophagus. As stated previously, the jejunum is anastomosed to the side of the undivided esophagus. It has been found by a number of observers that complete obstruction of the esophagus of dogs produces death in from one to three days. An entirely adequate explanation for this has never been advanced, but it is certain that both man and dog tolerate poorly division of the upper part of the esophagus.

Atresia

Congenital atresia of the esophagus with tracheoesophageal fistula has presented one of the most difficult problems in surgery. An illustration of this is presented in the report of Lanman²¹ of 32 patients with congenital atresia of the esophagus who were treated in the Children's Hospital in Boston. He stated: "In spite of the fatal outcome in all the 30 operative cases, it is felt that considerable progress along rational lines is being made. The successful operative treatment of a patient with this anomaly is only a question of time." It is only recently that the results have become encouraging. It has been almost five years since Leven performed the first of a number of operations on an infant with atresia who is now alive and well. Ladd²² has a total of 13 infants with congenital atresia of the esophagus who are alive, the oldest of these being four and a half years of age. Haight²³ has had remarkable success with the use of the ideal plan of extrapleural ligation of the fistula and primary anastomosis of the esophageal segments. This procedure was feasible in 17 of 24 infants in whom an exploration of the anomaly was performed. Six of the 16 patients in whom a primary anastomosis was performed are living from four and a half months to three years after operation, and all feedings are swallowed through the reconstructed esophagus. Several other surgeons, including Daniel,²³ have had success in a smaller number of patients.

It is likely that time and additional experience will show that primary anastomosis as used by Haight is the procedure of choice in those patients in whom the two ends of the esophagus can be brought together. On the other hand, improvements in methods for creating an artificial esophagus may point to the simpler procedure of bringing out

the upper and lower segments at the first operation under local anesthesia and subsequently performing a plastic procedure. The problem will probably be one of evaluating a higher earlier mortality rate associated with primary anastomosis as compared with a poorer functional result accompanying a delayed plastic procedure.

SURGERY OF THE LUNGS

Advances in surgery of the lungs have proceeded at a rapid pace, and no attempt will be made to consider them in detail. The increased use of the roentgen rays, lipiodol injection and the bronchoscope has resulted in earlier and more accurate diagnosis. Included among the functional tests that have been brought to a greater degree of perfection is bronchspirometry, by which the respiration of each lung can be measured.

Bronchiogenic carcinoma constitutes approximately 8 per cent of all carcinomas. It is only eleven years since the first one-stage removal of an entire lung was performed by Graham.²⁴ Shortly after this pneumonectomy for carcinoma, Rienhoff²⁵ removed an entire lung in a child. Graham²⁶ stated recently:

Rienhoff early demonstrated by his first case, in which the operation was carried out at almost the same time as my first case, that it is not necessary to perform a thoracoplasty in order to obliterate the pleural space and that individual ligation of hilar structures with a careful suturing of the bronchus has many advantages over the mass ligation of the hilar pedicle. These principles have now been generally accepted as procedures of choice. Total pneumonectomy, therefore, today usually means an operation for the complete removal of a lung, performed in one stage and with individual ligation of hilar vessels and suturing of the bronchus.

As is true in most well-conceived operative procedures, there has been a steady decline in the mortality rate associated with total pneumonectomy. At least part of this reduction is due to a realization of the futility of such an extensive procedure if there is much involvement of the mediastinal nodes, if there is bloody pleural fluid or if the phrenic or recurrent laryngeal nerve is paralyzed. Graham²⁶ has had a series of 104 patients in whom total pneumonectomy was performed, eighty-one of the operations being for neoplasms. The mortality rate in his last seventy cases for malignant neoplasms has been 30 per cent and that in the last 25 cases 12 per cent. Rienhoff²⁷ has performed eighty-six total pneumonectomies, sixty-four of which were for bronchiogenic carcinoma. His mortality rate during the last several years has been 12 per cent.

Total pneumonectomy has now been performed many times by many surgeons. Of greater importance than the steady reduction in the operative mortality rate is the fact that a number of the patients have shown no evidence of extension or metastasis. Furthermore, ordinary activities are very little restricted.

In a recent impressive personal experience, a right total pneumonectomy was performed for a large pulmonary metastasis that was detected more than four years after resection of the large bowel for carcinoma. The convalescence was uneventful and the patient left the hospital two weeks after the operation. He returned to work, but pneumonia developed in the remaining left lung four months after operation. This responded rapidly to sulfonamide therapy, and the patient left the hospital after a stay of one week. He returned to work one week later and has done well during the last three months. There has been a gain in weight of 11 pounds since the operation. When one recalls that it was twenty-five years after Billroth performed the first partial gastrectomy for cancer of the stomach before the procedure received any great attention, it is remarkable how rapidly and how widely total pneumonectomy has been accepted.

Suppurative disease of the lung and bronchiectasis in particular have constituted the most frequent single indication for lobectomy. The reduction in the mortality rate in recent years has been highly gratifying. Probably the chief factor in this reduction has been replacement of the massive hilar ligature by individual ligation of the vessels and a careful closure of the bronchus. A forward step was taken by Nelson,²⁸ by Churchill and Belsey²⁹ and by others when it was suggested that the bronchopulmonary segment should replace the lobe as the surgical unit of the lung. Probably everyone will agree that the removal of the diseased part should be accompanied by the conservation of as much normal pulmonary tissue as possible. Progress has also been made in the surgical treatment of other types of suppurative disease. An increasing number of chronic lung abscesses are being treated by lobectomy or pneumonectomy. Some cases of recurring unilateral pneumonitis and of lipoid pneumonia may be relieved by the same means. If congenital cystic disease is localized, the treatment consists of resection, preferably before infection has occurred. More than a year ago I performed a two-lobe lobectomy on the right side for congenital disease in an infant two months of age, and the result has been highly gratifying. It is the opinion of Gross³⁰ and of others that young children tolerate pulmonary resection satisfactorily.

One of the most important advances in the treatment of tuberculosis has resulted from an appreciation of the frequency of tracheobronchial infection and from the realization that this should be treated before collapse measures are employed. The indications for collapse therapy have been gradually extended and any patients who would previously have been treated by pneumothorax therapy are now being treated by thoracoplasty. The most significant recent change, however, has been in the increase in popularity of lobectomy and pneumonectomy in the treatment of pulmonary tuber-

is. Most of the early operations of this type performed because of a mistake in diagnosis. It was observed that many of the patients treated, surgeons were encouraged to use this method of therapy in treating certain patients with tuberculosis. Dolley and Jones³¹ stated in 1940 there is a definite place for lobectomy in certain cases and probably a place for pneumonectomy in a small group of cases. The main indications for these procedures have been considered to be the presence of strictures of bronchi that prevent adequate aeration and drainage, thick-walled uncolapsible cavities and tuberculous bronchiectasis. Churchill and Klopstock³² have recently reported cases in which patients with tuberculosis were treated by lobectomy. In 3 of these the orthodox indications for resection were present, whereas in the remaining 3 the usual indications for thoracoplasty existed but lobectomy was performed instead. Healing per primam occurred in all cases.

Churchill and Klopstock³² stated:

Lobectomy provides a more selective and immediate method of eradicating certain lesions of tuberculosis than does collapse therapy. It may be used subsequent to artificial pneumothorax, thereby restoring to that procedure the reputation of finesse that it should enjoy. A method of treatment that combines conservation of lung function, with immediate conversion of the sputum, and a shortening of the span of treatment cannot be dismissed until its scope has been more fully explored.

These authors,³² who make a sharp distinction in the indications for lobectomy and for pneumonectomy in the treatment of tuberculosis, write:

At the present time, total pneumonectomy cannot be considered an alternative to collapse therapy provided that collapse therapy is applicable to the case under consideration. It is both irreversible and nonselective. It irrevocably and seriously limits any therapeutic procedure that may be needed for the lung of the contralateral side. Circumscribed by strict indications, total pneumonectomy in tuberculosis may be a lifesaving operation when no other procedure is feasible. Lobectomy, on the other hand, is proposed as a highly selective measure for dealing with certain unilateral lesions. It is, indeed, far more conservative of pulmonary functions than even a seven-rib thoracoplasty.

During the last two years Overholt³³ in a few cases has deliberately elected pulmonary resection in preference to thoracoplasty. He has this to say regarding the use of lobectomy and pneumonectomy in the treatment of tuberculosis:

It can be definitely stated that the tuberculous subject and a patient with a positive sputum does not introduce any particular or unique hazards in regard to tissue healing. We can also state with certainty that the matter of resecting a tuberculous lung presents no unusual technical problem if the procedure is carried out as a primary form of treatment. The dissection of the hilum is carried out with probably greater ease than the dissection of the hilum in patients with suppurative disease or tumor. The problem of preventing contralateral spread still bothers us.

Overholt is of the opinion that pulmonary resection will not come to occupy so prominent a place in the treatment of tuberculosis as does pneumothorax

therapy or thoracoplasty. During a ten-year period he³³ and his associates have selected 94 patients in whom pulmonary resection was carried out, whereas well over 2000 patients have been treated by thoracoplasty during the same period. In 1942 and 1943 Overholt performed pulmonary resections on 59 patients with tuberculosis, with a mortality rate of 13 per cent. Pneumonectomy was performed in the majority of the cases. Since poor-risk patients were included, this accomplishment is an enviable one.

It is unnecessary to point out that the use of pulmonary resection in the treatment of pulmonary tuberculosis is in a formative stage. It is my opinion that the indications for resection are being extended too rapidly.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30331

PRESENTATION OF CASE

A twenty-four-year-old man entered the hospital because of shortness of breath, chest pain and inability to swallow.

The patient satisfactorily passed the Army induction examination twenty months before entry, but was discharged five months later. Eight months prior to admission, on examination for re-entrance into the Army, he was told that the x-ray films showed a tumor in the mediastinum. At that time he was asymptomatic, but within the next two months he noted a dull substernal pain on turning his head to one side and easy fatigability. He had considerable trouble swallowing solids, and moderate trouble with liquids. He developed a sensation of fullness in the throat and shortness of breath on exertion. One month before entry the substernal pain increased in frequency and severity, but still did not bother him especially. He had lost 20 pounds in eight months.

For eight years he had had a persistent hoarse voice, which he first noted following a sore throat. He had had occasional head colds and cough productive of whitish phlegm for several years.

Physical examination showed a well-developed, well-nourished man in no distress. The voice was hoarse, and there was an occasional cough. The heart and lungs were normal. There was no tracheal tug or increase in the mediastinal dullness. Moderate costovertebral-angle tenderness was present, but the abdomen was otherwise negative.

Laryngeal examination showed normal movement of the arytenoids and of the vocal cords. The cords did not completely occlude on adduction. There was slight thickening of the upper surface of the left cord, which prevented the cords from coming together. No evidence of active paralysis, any growth or tuberculosis was seen.

The blood pressure was 104 systolic, 46 diastolic, on the right, and 124 systolic, 60 diastolic, on the left. The temperature, pulse and respirations were normal.

Examination of the blood showed a white-cell count of 5800, with 70 per cent neutrophils. The

hemoglobin was 14.5 gm. per 100 cc. The urinalysis was normal. A blood Hinton test was negative.

X-ray examination of the chest showed the lungs to be clear throughout. The heart was normal in position, and the aortic knob was not visible in the posteroanterior projection. On the left side the hilar shadow was prominent, owing to a well-defined, round, soft-tissue mass measuring 3 cm. in diameter (Fig. 1). In the lateral and oblique views it appeared to be close to the aortic arch. Fluoroscopically it did not seem to pulsate. No displacement of the esophagus was seen. A barium swallow showed no delay in passage, and the outline of the esophagus was normal. Lateral films of the chest revealed the mass to lie just to the left and slightly anterior to the spine in relation to the descending aorta.

On the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. MERRILL C. SOSMAN†: The history makes one think immediately of mediastinal tumor, particularly with the report from the Army induction center that the x-ray films showed a tumor in the mediastinum. From what we see in the x-ray films the findings are out of proportion to the symptoms that this man presented. It is perfectly possible that a large part of these symptoms recorded were due to the fact that he was told at the induction center that the x-ray showed a tumor of the mediastinum. In other words, the dull substernal pain, the easy fatigability and the trouble with swallowing could all have been caused by pure nervousness, a psychologic upset because someone had told him that he had a tumor in the mediastinum. Aside from that I do not believe the history gives much of a lead. Occasionally, of course, a history alone makes the diagnosis. A classic example of that is angina pectoris. In fact, that is the only way one can make the diagnosis of angina pectoris in the majority of cases.

The physical examination is of no help. It was entirely negative except for the blood pressure, which was definitely lower on the right than on the left. I should like to know whether that was repeated and confirmed or whether it was a single observation.

DR. BENJAMIN CASTLEMAN: It is the only one recorded.

DR. SOSMAN: It is perfectly possible on a single examination to get a lower pressure on one side than on the other, again owing to psychic stimulus. The pain of pressure on one arm could excite the patient and give a higher reading in the second arm. A discrepancy of this sort should be checked and verified two or three times or on successive dates. This was only a single observation so far

†Roentgenologist, Peter Bent Brigham Hospital, clinical professor of roentgenology, Harvard Medical School

can tell, and it was the only positive physical finding in the entire examination. I doubt if the thickening of the upper surface of the left cord had any relation to the disease in this chest and I also doubt if the little lesion was seen in the x-ray examination was the cause of all the symptoms that are described. I would rather attribute these symptoms to nervous-

ness and worry in a man who had been told that he had a mediastinal tumor.

cannot be sure of the tumor shadow in the lateral and oblique views. It was probably observed and located fluoroscopically; by rotating the patient one can tell by the angle of disappearance how far forward or posteriorly the shadow is.

Can you see it any better than I can, Dr. Robbins?

DR. LAURENCE L. ROBBINS: I cannot see it anywhere except in the anteroposterior film. I think

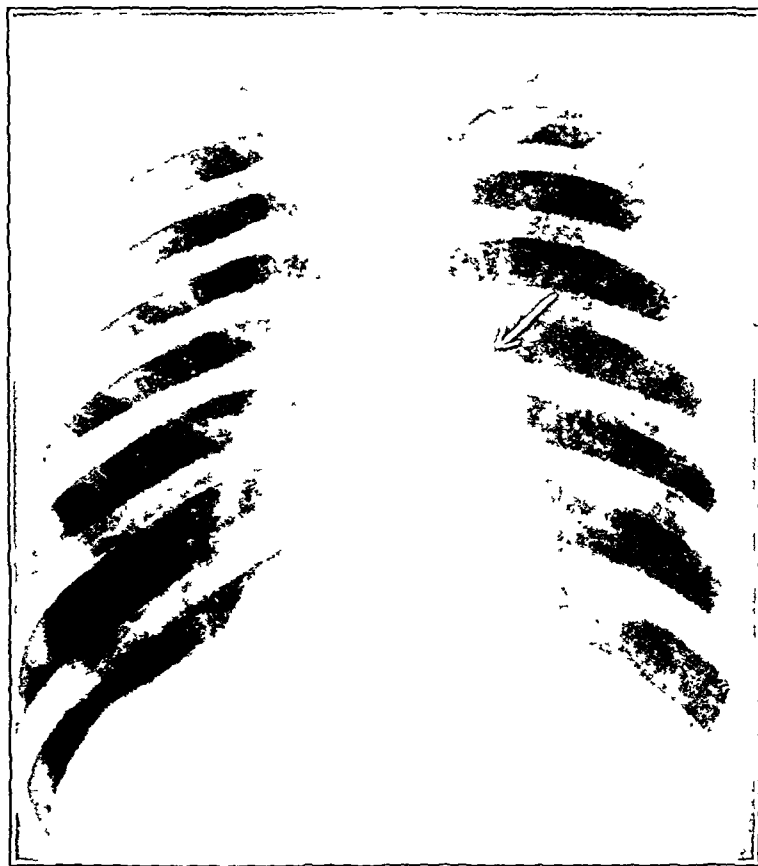


FIGURE 1

So far as these x-ray films are concerned, I must frankly admit that I had great difficulty in locating the small mass described in the lateral and oblique views. The anteroposterior view on fairly close scrutiny shows a normal chest, a small heart and a prominent pulmonary artery, which is seen in a great many individuals with ptotic hearts.

There is a little extra added here in the way of a double curve just below the pulmonary artery on the left border, projecting out in the region of the root of the left lung — a shadow that is about 2 cm. in width and 4 to 5 cm. in length. I stopped in the X-ray Department on my way over to see if Dr. Robbins could show the mass to me and he admitted that he could not see it. I frankly admit that I

that the statement must have been based on a fluoroscopic observation.

DR. SOSMAN: It is stated: "On the left side the hilar shadow was prominent, owing to an ill-defined, round, soft-tissue mass measuring 3 cm. in diameter. In the lateral and oblique views it appeared to be close to the aortic arch. Fluoroscopically it did not seem to pulsate. No displacement of the esophagus was seen. A barium swallow showed no delay in passage, and the outline of the esophagus was normal." The last statement indicates a rather striking discrepancy from the recorded symptoms of difficulty in swallowing, particularly the swallowing of solids.

The history certainly suggests a mediastinal tumor. The x-ray examination shows a very small, rather indeterminate shadow in the region of the

root of the left lung. It is hard to conceive how a shadow of that size and in that location could have given these symptoms. It is almost impossible to attribute the difference in blood pressure in the two arms to a small tumor in that location. If that discrepancy was real and not a faulty observation, one has to assume that it was caused by something else, perhaps a congenital anomaly of the blood vessels.

The possibilities in the way of diagnosis are legion. I do not know of any group of diseases that is more complex or variable than that of mediastinal tumors. These are divided into seven groups.

The first group comprises lymph nodes, the two main divisions being the inflammatory group and the neoplastic group, the latter primary and metastatic. The primary lesions, of course, are the malignant lymphomas. I do not believe that we can call these lymph nodes, either by their location or by their distribution. The patient had no evidence of infection to go with such a thing as tuberculosis or fungus infection or the nonspecific infections of lymph nodes. So I think we can rule out the lymph nodes, which are the commonest group of mediastinal tumors.

The second group consists of primary tumors of the mediastinum. The dermoids and the teratomas are nearly always in the anterior mediastinum. They are smooth, round, quite distinct in outline and quite unlike the appearance in this case. The ganglioneuromas and neurofibromas are usually posterior and arise from the intercostal nerves. Again, they are in a different location and have a different x-ray appearance from the shadow we see here. Occasionally we find the rare types, — the lipomas, the fibromas, the chondromas and even the cystic tumors (hygromas or lympho-angiomas), — none of which fit this particular picture.

The third group, infections in the mediastinum, I believe is ruled out. There is no evidence in the history or in the x-ray examination of an inflammatory process.

The thyroid tumors and thymomas come together in a single group. They are nearly always in the anterior and upper portions of the mediastinum, although they are occasionally found in the middle third, even as far down as the diaphragm, and are rarely found as an aberrant thyroid gland anywhere in the mediastinum.

Tumors of the esophagus, either the mucosal tumors or the extramucosal tumors of the esophageal wall, must be considered, although the fluoroscopist said that the esophagus was not displaced and there was no delay in the swallowing of barium. They most frequently occur in the middle third of the posterior mediastinum and sometimes have a slight attachment to the esophageal wall, and that slight attachment may be capable of causing symptoms without showing anything in the

x-ray examination in the way of a filling defect obstruction.

The tumors of the heart and aorta are next. I can rule out aneurysms and various tumors of the pericardium itself.

That leaves the bronchi as the only remaining source of origin for this tumor. We can rule out primary tumors of the bronchi. They are usually intrabronchial, and cough is the chief symptom. The patient's age is against it. He had no atelectasis, and no history of the raising of bloody sputum. In other words, all the symptomatology of carcinoma of the bronchus is missing, which does not rule it out to be sure, but is strongly against it. There are also the tumors that Dr. Robbins has described, bronchiogenic cysts, apparently embryonic tumors that develop cysts. These nearly always have smooth, round, distinct outlines, whereas this tumor, as I see it, has a serrated lobular outline. Then there is what has been called a "hamartoma," a fascinating tumor that I spring on every possible occasion to show my erudition. It is a congenital rest or bud, and in this particular case, a lung bud, presumably an aberrant lobe with undeveloped, collapsed lung containing recognizable lung tissue; it may become cystic, the cavity being lined with pulmonary or bronchial epithelium. Hamartomas and bronchial cysts overlap: some pathologists call them one thing and still others call them another, although "hamartoma" may be considered the basic classification for the entire group.

I shall summarize by saying that this patient had a small indefinite mediastinal mass. Since I have ruled out most of the possibilities that I had listed, I suggest that it was either one of the bronchiogenic cysts (hamartoma) or one of the duplications of the gastrointestinal tract, a cyst attached to the esophagus. I rather favor the former because fluoroscopy showed nothing in the esophagus. I should be interested to know what the x-ray interpretation was.

DR. CASTLEMAN: Dr. Davis's interpretation on fluoroscopy was that it had the appearance of an enlarged lymph node, fitting in with the first of your seven groups.

CLINICAL DIAGNOSIS

Neurofibroma of posterior mediastinum.

DR. SOSMAN'S DIAGNOSIS

Hamartoma of left lung (undeveloped lung bud).

ANATOMICAL DIAGNOSIS

Sarcoid of mediastinal lymph nodes.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: I am sorry that Dr. Sweet is not here to describe the operative findings. His

eads: "One large, irregular, dark gray mass was removed from under the arch of the and another, measuring 2 by 3 cm., from the e above the arch of the aorta. Two other nodes' were left behind." Apparently the first that Dr. Sweet refers to is that represented shadow with the serrated border indicated by row in the roentgenogram of the chest (Fig. 1). Microscopic examination showed that these s were lymph nodes almost completely red by sarcoid.

I suppose that it is quite possible that the films by the Army showed a larger mass and that e time of operation the sarcoid was in the ss of regression. We know that in most cases sarcoid the mediastinal nodes regress after a od of time; there is another group, however, progress to involve the lung parenchyma itself. general belief is that the mediastinal nodes be e involved first and that involvement of the ; parenchyma is secondary. One ordinarily ks of enlarged lymph nodes as being secondary : neighboring lesion but a great many cases have n reported, especially from Sweden,² and we e had several here, that showed primary enge- ment of hilar nodes followed by parenchymal ase. Has that been your experience, Dr. Sosman?

DR. SOSMAN: Yes; first the hilar nodes, and then rograde lymphatic spread into the lungs.

DR. CASTLEMAN: The same principle of retro- de lymphatic spread probably occurs in metas- ic carcinoma to the mediastinal nodes from cer of the stomach or other extrapulmonary cinomas. In other words so-called "lymphatic ead" of pulmonary metastases may begin in the ph nodes and extend into the lung parenchyma her than drain from the lung into the lymph les.

Dr. Ronald C. Sniffen has recently reviewed our es of metastatic pulmonary carcinoma with H. P. Mueller of the X-ray Department.³ They lieve that the lymphatic spread of carcinoma has characteristic x-ray pattern and that in many es it develops by retrograde extension from the ar lymph nodes.

DR. SOSMAN: We have seen it occasionally, but is rare.

Do you believe that this small group of lymph des involved with sarcoid could have accounted r all this patient's symptoms.

DR. CASTLEMAN: No, unless they were larger one time. It would be interesting to find out hether the blood-pressure readings were repeated d found to be different on the two sides. I do not lieve that pressure on the vessels by these nodes ould have caused a difference in the blood pressure the two arms.

DR. SOSMAN: The most striking thing about roid, in my experience, and a valuable point in aking the diagnosis, is the marked discrepancy tween the extensive pulmonary involvement,

including the hilar and mediastinal nodes, that is usually present and the paucity of symptoms. Patients do not have symptoms with sarcoid. Here there was slight involvement and marked symptoms. The symptoms suggest that he was worried about his condition.

DR. JOSEPH C. AUB: Was the plasma protein ever determined?

DR. SOSMAN: And the globulin?

DR. CASTLEMAN: No. It would also be interesting to know the results of a tuberculin test.

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CASE 30332

PRESENTATION OF CASE

A seventy-seven-year-old retired domestic entered the hospital because of hemoptysis and sudden chest pain.

The history was quite inadequate. The patient had apparently been in good health until two or three months prior to entry, at which time she complained of dull pain in the lower right chest. She was apparently able to carry on until two days before entry, when she experienced a sudden "crack" in the region of the lower right costal margin. This was followed by pain that persisted, according to the record, "as a severe episodic form of pain exaggerated by respirations." She developed a cough productive of blood-streaked or rusty sputum. The abdomen became distended, and swelling of the ankles developed. She was unable to sleep or eat. She had no true chills but several "sieges of trembling."

The past history was essentially negative. She had slept on two pillows all her life.

Physical examination showed an emaciated, cyanotic, dehydrated woman. The skin was warm and dry. The lips and tongue were dry. Chest expansion was poor on the right with dullness and decreased breath sounds, voice sounds and tactile fremitus over the lower half. Coarse moist rales were heard over the upper half of both lungs. The heart was of normal size. The sounds were of fair quality, and there were occasional extrasystoles. The abdomen was distended and taut. Slight pitting edema of the ankles was noted.

The blood pressure was 120 systolic, 60 diastolic. The temperature was 104°F., the pulse 130, and the respirations 30.

Examination of the blood showed a red-cell count of 4,050,000, with 13.9 gm. of hemoglobin. The white-cell count was 21,800, with 88 per cent neutrophils, of which 80 per cent were band forms and 8 per cent myelocytes. There was marked

CLINICAL DIAGNOSIS

Lobar pneumonia.

DR. HARWOOD'S DIAGNOSIS

Carcinoma of bronchus, with secondary pneumococcal infection.

ANATOMICAL DIAGNOSES

Lobar pneumonia (Friedländer's bacillus).

Bacteremia (Friedländer's bacillus).

Duodenal ulcer, acute.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy we found about 100 cc. of turbid fluid in the right pleural cavity and a similar amount on the left side. The mass seen by x-ray proved to be a consolidated right lower lobe which on section was soft and brownish gray and on scraping the surface a large amount of mucoid material was obtained. Cultures from the lung and heart's blood showed the typical mucoid Friedländer's bacillus. The fact that the patient died twenty-four hours after admission, two days after

the onset of symptoms, fits in with the usual course of the Friedländer type of pneumonia. Most of the patients die within a few days, although a few develop abscesses and have recurrent attacks of pneumonia. We were unable to find an encapsulation of the fluid, although there were some old adhesions on the right side. The cause of the positive guaiac test on the stools was a small duodenal ulcer.

DR. SOSMAN: That round shadow is the apex of the consolidated right lower lobe?

DR. CASTLEMAN: I should think so.

DR. HARWOOD: What did the ante-mortem culture show?

DR. CASTLEMAN: Friedländer's bacillus, but growth had not occurred until after the patient's death. In retrospect, the organisms seen by the house officer were Friedländer's bacilli, which are gram negative, not pneumococci, which are gram positive.

DR. HARWOOD: I had considered Friedländer's pneumonia because in that condition death is usually early and distention of the abdomen is a prominent feature, but ruled out the diagnosis because of the bacteriologic findings that were reported.

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PRESCRIPTION OF HEAVY CREAM

LAST week the *Journal* took editorial notice of one of the more recent *causes célèbres* — Amendment 2 to War Food Order 13, emanating from the Office of Distribution of the War Food Administration. According to this amendment, medical prescriptions for heavy cream must be approved by the public-health officer or the secretary of the county medical society of the area where a patient or hospital is situated.

In Massachusetts, authority has been given to the district supervisor of the Office of Distribution to make a reasonable interpretation of the terms of the amendment, to the extent that not only will

the broad purposes of the order be better served but practicing physicians will be relieved of the irritation of having their prescriptions subject to the endorsement of a variety of persons. The endorsing function has, by this interpretation, been vested in an advisory committee composed as follows: John H. Sullivan, district supervisor, Office of Distribution, War Food Administration, chairman; Dr. Vlado A. Getting, commissioner of public health, Commonwealth of Massachusetts; Dr. G. Lynde Gately, health commissioner, City of Boston; Dr. H. Quimby Gallupe, secretary, Board of Registration in Medicine; Dr. Nathaniel W. Faxon, director, Massachusetts General Hospital; and Drs. F. Gorham Brigham, Joseph Garland, Loring Grimes and Franklin W. White, representing the Massachusetts Medical Society.

Prescriptions, which are valid for a period not exceeding sixty days, should indicate the date of issuance, the butter-fat content required, the daily quantity required and the necessity of such cream for medical treatment, and should be forwarded to the War Food Administration, 404 Park Square Building, Boston. Telephone inquiries should also be directed to the Food Distribution Administration (LIBerty 7520).

It is apparent that few prescriptions will receive the endorsement of this committee in view of the overwhelming mass of evidence that cream in excess of 19 per cent butter fat is rarely, if ever, a necessity in medical treatment. Milk, in these critical days, needs to be conserved. One of the best ways of conserving it in order that we may have enough fluid and dried milk, butter, cheese and light cream, is practically to abolish, for the time being, the luxury of heavy cream.

An appeal to the patriotism of patients should be almost sufficient to eliminate the demand for heavy cream.

RED-CELL RESIDUES

THE organization and rapid growth in the last three years of the Blood-Donor Service of the American Red Cross has been one of the miracles of this country's ability to produce for war. During the interval between the two world wars it became evident that restoration of blood volume with plasma

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DESCRIPTION OF HEAVY CREAM

LAST week the *Journal* took editorial notice of one of the more recent *causes célèbres* — Amendment 2 to War Food Order 13, emanating from the Office of Distribution of the War Food Administration. According to this amendment, medical prescriptions for heavy cream must be approved by the public-health officer or the secretary of the county medical society of the area where a patient or hospital is situated.

In Massachusetts, authority has been given to the district supervisor of the Office of Distribution to make a reasonable interpretation of the terms of the amendment, to the extent that not only will

the broad purposes of the order be better served but practicing physicians will be relieved of the irritation of having their prescriptions subject to the endorsement of a variety of persons. The endorsing function has, by this interpretation, been vested in an advisory committee composed as follows: John H. Sullivan, district supervisor, Office of Distribution, War Food Administration, chairman; Dr. Vlado A. Getting, commissioner of public health, Commonwealth of Massachusetts; Dr. G. Lynde Gately, health commissioner, City of Boston; Dr. H. Quimby Gallupe, secretary, Board of Registration in Medicine; Dr. Nathaniel W. Faxon, director, Massachusetts General Hospital; and Drs. F. Gorham Brigham, Joseph Garland, Loring Grimes and Franklin W. White, representing the Massachusetts Medical Society.

Prescriptions, which are valid for a period not exceeding sixty days, should indicate the date of issuance, the butter-fat content required, the daily quantity required and the necessity of such cream for medical treatment, and should be forwarded to the War Food Administration, 404 Park Square Building, Boston. Telephone inquiries should also be directed to the Food Distribution Administration (LIBerty 7520).

It is apparent that few prescriptions will receive the endorsement of this committee in view of the overwhelming mass of evidence that cream in excess of 19 per cent butter fat is rarely, if ever, a necessity in medical treatment. Milk, in these critical days, needs to be conserved. One of the best ways of conserving it in order that we may have enough fluid and dried milk, butter, cheese and light cream, is practically to abolish, for the time being, the luxury of heavy cream.

An appeal to the patriotism of patients should be almost sufficient to eliminate the demand for heavy cream.

RED-CELL RESIDUES

THE organization and rapid growth in the last three years of the Blood-Donor Service of the American Red Cross has been one of the miracles of this country's ability to produce for war. During the interval between the two world wars it became evident that restoration of blood volume with plasma

or serum was the *sine qua non* of the treatment of shock, and the large supply of plasma now available to our armed forces is the result of careful and long-sighted planning.

During the course of World War II interest has been aroused in some of the constituents of the blood other than plasma itself. This has been true of the red-cell residues following the removal of plasma from a blood donation. Soon after the organization of the Blood-Donor Service it became apparent that the loss of red-cell residues was a frank waste of an important part of the donor blood. Furthermore, as experience with war casualties grew, a need for the red-cell component of blood, as well as the plasma, became evident. Red cells have been supplied so far to our troops overseas by whole blood drawn for the purpose at the time and place it was to be used. The use of red-cell residues at the front has been limited by the poor storing qualities, so that even with air-borne transportation it has not been practical to use them.

Red-cell residues have been made available, however, to certain hospitals in the United States for civilian use. Taylor, Thalhimier, and Cooksey¹ report the administration of eighteen thousand transfusions using red-cell residues resuspended in physiologic saline solution. Their work has confirmed, on a much larger scale, the experience of many others who have in recent years shown that suspensions of red cells may, with certain limitations, be used in the treatment of anemia.

The red-cell suspensions so used furnish all the important elements for the replacement of erythrocytes. The chief advantage of their use is that the plasma is saved for other purposes. Another advantage is that, by suspending the erythrocytes in a smaller amount of fluid than that necessary to restore the original volume, a transfusion medium is made that contains less sodium chloride and more hemoglobin than a whole-blood transfusion. This procedure is particularly useful in patients with severe anemia and congestive cardiac failure, in whom it is urgently desirable to raise the hemoglobin and red-cell count and to reduce the blood volume and body salt. Red-cell suspensions made in this way, however, remain usable for a much

shorter period of time than those resuspended their original volume in physiologic saline solution or in one of the newer fluids.

The storage of red-cell suspensions has been studied for a number of years, but research has been greatly stimulated by the quantities now available as well as by the possibility that, with air-borne transportation, the cells might be used by the armed forces overseas if their life in storage could be prolonged. Investigators have been searching for the ideal resuspending fluid — one that would prevent increased fragility of the cells to hypotonic solutions, that could be given without fear of untoward reaction and that would, if possible, promote the longevity of the cells after administration. Solutions containing various combinations of electrolytes, and usually glucose, have been extensively studied regarding both the prevention of hemolysis in vitro and the duration of life of the cells in vivo. Denstedt et al.,² after much painstaking work, proposed a fluid containing 2.3 per cent glucose and 1.7 per cent sodium citrate, buffered to pH 7.4 with sodium phosphate. Using red cells tagged with radioactive iron, Ross³ and others⁴ have found that cells resuspended in Denstedt's fluid, or a similar mixture, can be stored for two weeks, or perhaps longer, with 80 to 90 per cent of the cells surviving forty-eight hours after transfusion. Although further studies are necessary, this is an indication of the possibilities of the use of red-cell suspensions.

The separation of blood into its physiologically active components offers new opportunities for the blood bank of the future. One might think of each community with a blood-donor service prepared to supply whole blood, plasma, albumin, specific globulin fractions and erythrocyte suspensions. The proper use of such a service would require the cooperation of the physicians within the community, but the therapeutic possibilities are manifold.

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The need for some system of food rationing made itself felt in the first year of war, when it became apparent that shortages of certain foods would give rise to inequalities of distribution and resultant hoarding, and might even cause their disappearance from the market. These shortages were due to two obvious causes—a tendency to decreased production as a result of insufficient labor and material, and an increased consumption because of the growth of the armed services and the demands of lend lease. On March 1, 1943, consequently, some months after sugar rationing had been put into effect, a point system of rationing for many meats, fats and processed foods was established.

Rationing under any circumstances is subject to difficulties: man is ever mindful of his own, and war always presents the contrasts of great sacrifices and great selfishness. In this country its difficulties are increased by the peculiarities of our national situation. We are a food-producing country, with a fixed population of diverse dietary habits. Seasonal differences in food supply exist, making uniform rationing regulations inconsistent, and we have experienced, on the home front, an almost complete immunity to the perils of war.

Nevertheless, even with the relatively mild degree of food rationing to which we have so far been subjected, there was early recognized the possible need for special consideration of certain patients and institutions on account of health requirements, in order to safeguard in theory, and in practice so far as possible, the rights of all. Consequently in April, 1943, the director of the War Food Administration requested the National Research Council to appoint "a group of nationally known physicians to advise the War Food Administration concerning the extent of these special needs and the best method of meeting them."

The Subcommittee on Medical Food Requirements of the Committee on Drugs and Medical Supplies within the Division of Medical Sciences of the Council resulted. This committee studied the problem during the next few months, and published its report in the October 16 issue of the *Journal of the American Medical Association*.

The recommendations of this report form the basis on which departures from strict adherence to food rationing are made on medical grounds. They limit and interpret the list of conditions for which extra rations are allowable, and the quantities of extra rations allowed, yet guard against too strict an interpretation of their policies. Liberal interpretations may be made of the principles involved, but in order that the affairs of the public

should be protected, it is further suggested that the flexibility of the program be vested in medical panels appointed to aid the state or regional rationing boards in the discharge of these particular duties.

Massachusetts, one of the first of the states to recognize the desirability of such an organization, responded with a committee appointed in June, 1943, by the president of the Massachusetts Medical Society at the request of the director of the State Office of Price Administration.

The recommendations of the subcommittee of the National Research Council, although published in October, 1943, and utilized since that time as a guide for procedure, were not accepted and put into effect by the Office of Price Administration until March 30, 1944. These recommendations, in substance, permit extra rations within qualitative and quantitative limitations for the following conditions: diabetes mellitus, active tuberculosis, chronic nephritis of the nephrotic type, cirrhosis of the liver, severe hepatitis, chronic suppurative diseases, burns, gastrointestinal lesions and pregnancy. As has been stated, these recommendations may require liberal interpretation.

Certain fundamental difficulties soon become apparent in any effort to establish a program for supplying extra rations for the sick. The need for rationed foods must obviously depend on the availability of nonrationed foods, not only as regards their actual scarcity, but also as regards their expense and their nutritional substitution value for rationed foods, due consideration being given to seasonal and geographical variations in their supply.

Since point values vary on different forms of rationed foods even inside the various groups and classes, the availability of rationed foods must also be considered in terms of local conditions of supply and demand, prices and number of ration books in a family. A person has much greater difficulty in constructing an adequate diet with one ration book, than does the marketer for a family that can pool a number of ration books in buying on a quantity basis. The frequent shifting of point values on rationed foods, depending on their nationwide availability, also creates problems that make any rigid allowances inaccurate and often inconsistent with the needs of the case.

These difficulties are implicit in the very nature of food rationing and are due largely to its elasticity—an elasticity that is vitally necessary if rationing is to be just but one requiring an equal elasticity in its modifications.

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dietary habits and racial peculiarities as it was for Procrustes to try and fit his unhappy lodgers into his single bed of fixed dimensions. Moreover, despite the prodigious advances that have been made in our knowledge of the role of diet in health and disease since Captain Cook first demonstrated the need of fresh foods on an ocean voyage, our information regarding the specific role of diet in many diseases can scarcely be considered mathematical.

With this inexactness of knowledge, there are still permissible wide variations in the views of individual physicians regarding the part that diet may play in the treatment of certain diseases, and it is frequently on the statements of these physicians that judgments must be made on the allotments requested for individual cases, in order to do justice to both the patient and the public. It must be recognized, too, that few physicians can have the information on food values and their seasonal irregularities that would be necessary for an accurate month-by-month appraisal of their patients' needs.

Strictness in the interpretation of regulations applying to extra rations must also be a variable factor, depending on the month-by-month needs of rationing. We must also bear in mind that few patients actually require more food or different food than can be obtained from their basic allotments and point-free foods, that many average-sized families do not find it necessary to use up their basic allotments, and that many active medical practitioners rarely, if ever, find it necessary to prescribe extra food allotments for their patients.

The committee appointed in this state to aid the district rationing executive had little in the way of precedent to help it in its early deliberations. After consulting authorities in various fields of medicine, however, it was decided to accept as a reasonable maximum for any diagnosis the allotments of rationed foods that had been determined as a reasonable maximum for patients with diabetes, namely, 4 pounds of processed foods and 5 pounds of meats and fats per week. These amounts include the basic rations, but do not include unrationed foods. As later developments showed, this allotment compares favorably with the diets recommended for diabetes and other diseases by the subcommittee of the National Research Council. A smaller allotment (2 pounds of processed foods and 3 pounds of meats and fats per week) was later adopted and allowed where need seemed to exist in conditions not accepted by the subcommittee of the National Research Council or where any doubt existed concerning the needs of the patient. When point values were removed from many meats these allowances were halved for meats and fats, and are continually subject to revision as conditions change.

The impossibility of attaining mathematical accuracy in the task of attempting to temper the wind

to the shorn lamb has been indicated. The best any advisory group can do is to profit by its experience, to try and keep abreast of change, improve its methods of administration in a where so little exact knowledge exists, and to rely on continuous flexibility of a program that with so many variable factors.

Figures at present available indicate that approximately 13,500 persons in Massachusetts are receiving supplemental rations, or 0.3 per cent of population. This does not seem to be an unhigh figure, but it does suggest a considerable number who have sought and failed to receive extra allotments. These requests are for a variety of conditions, some of which are patently unsuited to dietary treatment, and some of which could not reasonably be expected to be met from it according to accepted standards of treatment; they are made not infrequently for gargantuan quantities of food, the ingestion of which some patients could hardly be expected to survive.

Success in the limitation of extra allotment food to those relatively few persons who absolutely require it must depend in large measure on knowledge and integrity of practicing physicians. Admitting differences in methods of treatment in the patients treated, and taking into consideration the limitations of our knowledge, we believe nevertheless that the restrictions as established are fair ones.

It would help the committee if the physicians' statements in requesting extra food were fuller and more accurate. This would avoid long delays to the patient, occasioned by asking for further information from the doctor. For example, the committee needs more exact diagnoses; not simply "anemia," but the kind and severity; not simply "hematemesis," but the date and the existing level of hemoglobin; not simply "operation," but the date and kind. It still seems as if the number of requests for extra food was far too high and could be greatly lessened if the doctor would look at his patient more critically and ask himself if the extra ration was really a medical necessity in cases such as hemiplegia, "rheumatism," concussion, skin disease, psychoneurosis, angina, ptosis, asthenia, Parkinson's disease, irritable colon, heart disease and so forth.

The work of the advisory committee will be further expedited as information concerning rationing activities becomes more general. For months it has been found necessary to enlist its aid in the rationing problems of the other New England states except Rhode Island, due to the absence of committees in these states. It will be able to do its work more effectively when relieved of these burdens and when local committees are established, as is now planned, to work in conjunction with the rationing boards in various key cities.

JOSEPH GARLAND, *Chairman*

(Notices on page xiii)

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AIN AND DISABILITY OF SHOULDER AND ARM DUE TO HERNIATION OF THE NUCLEUS PULPOSUS OF CERVICAL INTERVERTEBRAL DISKS*

JOST J. MICHELSEN, M.D.,† AND WILLIAM J. MIXTER, M.D.‡

BOSTON

THE clinical picture of a rupture of an intervertebral disk in the lower lumbar region has become a well-defined entity within the last few years.^{1,2} Its symptoms and signs of root compression are characteristic and easily recognized. The presence and level of the lesion can be demonstrated by lipiodol,³ which is removed after the x-ray examination.⁴ The surgical treatment of what seemed not so long ago to be "intractable sciatica" gratifying, and the number of cases successfully diagnosed and relieved is increasing steadily.

Herniation of the nucleus pulposus in the cervical region is considered to be rare. Stookey⁵ in 1927 described a group of unusual so-called "tumors" arising from the cervical intervertebral disk, and reviewed the subject thirteen years later.⁶ He distinguished three different syndromes of cervical-disk herniation: the syndrome of bilateral ventral pressure (3 cases), that of unilateral ventral pressure (3 cases) and that of nerve-root pressure (1 case). In the majority of his cases, and in those reported by Mixter and Ayer⁷ and other observers,^{8,9} the herniated cartilage produced compression of the cord. This led to the belief that the symptomatology of disk herniation in the cervical and in the lumbar region are fundamentally different. Stookey also concluded from his observations that the operative results in cervical herniations are not too encouraging.

There is evidence that cord compression as a diagnostic criterion of cervical herniation has been overemphasized. In our experience lesions of cervical disks produced compression of the cord in 6 cases, and involvement of nerve roots was the predominant feature in 8 cases. Stookey described the picture of root compression as consisting of muscle atrophy and hypotonia, limited to the dis-

tribution of the roots involved and producing purely subjective sensory symptoms, such as burning, gnawing and tingling, which may be increased by movement of the extremity.

Spurling's¹⁰ patient complained of severe pain in the lower neck and tip of the shoulder and pain and inability to abduct the left arm. The onset of the disability was preceded by a "strain of the neck." The pain was exacerbated by sneezing, coughing and straining. On the first admission tenderness of the fifth and sixth cervical spinous processes and hypesthesia in approximately the fifth cervical dermatome over the tip of the shoulder were found. Nine years later there was atrophy of the left deltoid and infraspinatus muscles and inability to abduct the left arm, in addition to the sensory changes previously observed. The total protein in the cerebrospinal fluid was 80 mg. per 100 cc. A doubtful filling defect on the left between the sixth and seventh cervical vertebrae was seen on lipiodol examination. Laminectomy revealed a mass compressing the sixth cervical nerve root against the overlying ligamentum flavum. It was not removed because "direct attack on the protrusion would have led to damage to the nerve and possibly the spinal cord." The decompression gave relief of symptoms.

Hanflick¹¹ described a case with a herniated nucleus pulposus at the sixth cervical interspace. The patient complained of pain, aggravated by coughing, sneezing and straining, in the left side of the neck, left costocoracoid area, left arm, left forearm and second and third fingers, with paresthesias of these two fingers — hyperesthesia to pinprick and hypesthesia to touch and vibration. The total protein in the cerebrospinal fluid was 83 mg. per 100 cc. Fluoroscopy after lipiodol injection disclosed an extramedullary lesion between the sixth and seventh cervical vertebrae. Laminectomy and removal of the disk fragment gave complete relief of symptoms. Head traction had previously been used without effect.

*Presented at the meeting of the Boston Orthopedic Club, October 18, 1943.
†From the Neurosurgical Service, Massachusetts General Hospital and the Department of Surgery and the Department of Neurology, Harvard Medical School.

‡Assistant neurosurgeon, Massachusetts General Hospital, instructor in neurology and assistant in surgery, Harvard Medical School.
§Consulting neurosurgeon, Massachusetts General Hospital.

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The impossibility of attaining mathematical accuracy in the task of attempting to temper the wind

to the shorn lamb has been indicated. The best that any advisory group can do is to profit by its own experience, to try and keep abreast of changes and improve its methods of administration in a field where so little exact knowledge exists, and to insist on continuous flexibility of a program that deals with so many variable factors.

Figures at present available indicate that approximately 13,500 persons in Massachusetts are receiving supplemental rations, or 0.3 per cent of the population. This does not seem to be an unduly high figure, but it does suggest a considerably greater number who have sought and failed to receive extra allotments. These requests are made for a variety of conditions, some of which are patently unsuited to dietary treatment, and others of which could not reasonably be expected to benefit from it according to accepted standards of treatment; they are made not infrequently for gargantuan quantities of food, the ingestion of which some patients could hardly be expected to survive.

Success in the limitation of extra allotments of food to those relatively few persons who absolutely require it must depend in large measure on the knowledge and integrity of practicing physicians. Admitting differences in methods of treatment and in the patients treated, and taking into consideration the limitations of our knowledge, we believe nevertheless that the restrictions as established are fair ones.

It would help the committee if the physicians' statements in requesting extra food were fuller and more accurate. This would avoid long delays for the patient, occasioned by asking for further information from the doctor. For example, the committee needs more exact diagnoses: not simply "anemia" but the kind and severity; not simply "hematemesis," but the date and the existing level of the hemoglobin; not simply "operation," but the date and kind. It still seems as if the number of requests for extra food was far too high and could be greatly lessened if the doctor would look at his patient more critically and ask himself if the extra ration is really a medical necessity in cases such as hemiplegia, "rheumatism," concussion, skin disease, psychoneurosis, angina, ptosis, asthenia, Parkinson's disease, irritable colon, heart disease and so forth.

The work of the advisory committee will be further expedited as information concerning its activities becomes more general. For months it has been found necessary to enlist its aid in the rationing problems of the other New England states except Rhode Island, due to the absence of committees in these states. It will be able to do its work more effectively when relieved of these burdens, and when local committees are established, as is now planned, to work in conjunction with the rationing boards in various key cities.

JOSEPH GARLAND, *Chairman*

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PAIN AND DISABILITY OF SHOULDER AND ARM DUE TO HERNIATION OF THE NUCLEUS PULPOSUS OF CERVICAL INTERVERTEBRAL DISKS*

JOST J. MICHELSEN, M.D.,† AND WILLIAM J. MIXTER, M.D.‡

BOSTON

THE clinical picture of a rupture of an intervertebral disk in the lower lumbar region has become a well-defined entity within the last few years.^{1,2} Its symptoms and signs of root compression are characteristic and easily recognized. The presence and level of the lesion can be demonstrated by lipiodol,³ which is removed after the x-ray examination.⁴ The surgical treatment of what seemed not so long ago to be "intractable sciatica" is gratifying, and the number of cases successfully diagnosed and relieved is increasing steadily.

Herniation of the nucleus pulposus in the cervical region is considered to be rare. Stookey⁵ in 1927 described a group of unusual so-called "tumors" arising from the cervical intervertebral disk, and reviewed the subject thirteen years later.⁶ He distinguished three different syndromes of cervical-disk herniation: the syndrome of bilateral ventral pressure (3 cases), that of unilateral ventral pressure (3 cases) and that of nerve-root pressure (1 case). In the majority of his cases, and in those reported by Mixter and Ayer⁷ and other observers,^{8,9} the herniated cartilage produced compression of the cord. This led to the belief that the symptomatology of disk herniation in the cervical and in the lumbar region are fundamentally different. Stookey also concluded from his observations that the operative results in cervical herniations are not too encouraging.

There is evidence that cord compression as a diagnostic criterion of cervical herniation has been overemphasized. In our experience lesions of cervical disks produced compression of the cord in 6 cases, and involvement of nerve roots was the predominant feature in 8 cases. Stookey described the picture of root compression as consisting of muscle atrophy and hypotonia, limited to the dis-

tribution of the roots involved and producing purely subjective sensory symptoms, such as burning, gnawing and tingling, which may be increased by movement of the extremity.

Spurling's¹⁰ patient complained of severe pain in the lower neck and tip of the shoulder and pain and inability to abduct the left arm. The onset of the disability was preceded by a "strain of the neck." The pain was exacerbated by sneezing, coughing and straining. On the first admission tenderness of the fifth and sixth cervical spinous processes and hypesthesia in approximately the fifth cervical dermatome over the tip of the shoulder were found. Nine years later there was atrophy of the left deltoid and infraspinatus muscles and inability to abduct the left arm, in addition to the sensory changes previously observed. The total protein in the cerebrospinal fluid was 80 mg. per 100 cc. A doubtful filling defect on the left between the sixth and seventh cervical vertebrae was seen on lipiodol examination. Laminectomy revealed a mass compressing the sixth cervical nerve root against the overlying ligamentum flavum. It was not removed because "direct attack on the protrusion would have led to damage to the nerve and possibly the spinal cord." The decompression gave relief of symptoms.

Hanflig¹¹ described a case with a herniated nucleus pulposus at the sixth cervical interspace. The patient complained of pain, aggravated by coughing, sneezing and straining, in the left side of the neck, left costocoracoid area, left arm, left forearm and second and third fingers, with paresthesias of these two fingers — hyperesthesia to pinprick and hypesthesia to touch and vibration. The total protein in the cerebrospinal fluid was 83 mg. per 100 cc. Fluoroscopy after lipiodol injection disclosed an extramedullary lesion between the sixth and seventh cervical vertebrae. Laminectomy and removal of the disk fragment gave complete relief of symptoms. Head traction had previously been used without effect.

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From the Neurosurgical Service, Massachusetts General Hospital and the Department of Surgery and the Department of Neurology, Harvard Medical School.

†Assistant neurosurgeon, Massachusetts General Hospital, instructor in neurology and assistant in surgery, Harvard Medical School.

‡Consulting neurosurgeon, Massachusetts General Hospital.

Semmes and Murphey¹² observed a group of 4 cases with apparent unilateral rupture of the sixth cervical disk, in 3 of which this diagnosis was proved at operation. They proposed a syndrome characterized by pain in the neck, shoulder, precordium and arm and by sensory changes in the index and middle fingers. The pain was made worse by sneezing, coughing and straining and by movements of the neck. The important findings on examination included tenderness over the exit of the seventh cervical nerve root from the spinal canal and over the scapula, hypesthesia in the index finger, slight reduction of sensibility of the middle finger, normal arm and leg reflexes and absent cervical lordosis on the x-ray films. The total protein was increased in 2 cases. No lipiodol examinations were performed. The site of the lesion was localized during the operation, which was carried out under local anesthesia. Gentle pressure on the ligamentum flavum reproduced the pain, and novocain infiltration of the corresponding nerve root abolished it. Two of these patients were completely relieved.

The present report is based on experiences with 8 cases, all of which were proved pathologically at operation. There were lesions at the fifth cervical interspace in 4 cases, at the sixth in 3, and at the seventh in 1, with encroachment on the sixth, seventh and eighth cervical nerve roots, respectively.

CASE REPORTS

CASE 1 (M. G. H. 334269). A. T. S., a 45-year-old unemployed weaver, was admitted to the Massachusetts General Hospital for the second time in April 23, 1934, because of pain and weakness of left shoulder and arm. Twenty-two months prior to admission, a crank he was turning to raise the body of a dump car slipped and struck his left arm just below the deltoid muscle. There was local pain for several days. Eleven months later pain and numbness began in the anterolateral left upper arm, antecubital region and forearm; it was made worse by movements of the arm, which became weaker and smaller.

Examination revealed atrophy of the left upper arm, particularly of the deltoid and biceps. There were muscle twitchings of the deltoid. The arm reflexes were apparently equal, the left knee jerk was more active than the right, and the left plantar response was equivocal. There was hyperesthesia to pinprick and temperature in the antecubital region and a small area above the spine of the scapula. A lumbar puncture showed a protein level of 43 mg. per 100 cc. The cisternal fluid contained 24 mg. The dynamics were equivocal. A lipiodol examination was unsuccessful because the lipiodol could not be moved from the cistern.

At operation a hard, fibrous mass of tissue 1.0 cm. in diameter and 0.2 cm. in thickness was found between the 5th and 6th cervical vertebrae impinging on the cord. Because of brisk bleeding it was not removed. On later check-up examination the patient was found to have weakness of the biceps and deltoid but was able to do odd jobs.

CASE 2. (M. G. H. 27277). O. A., a 49-year-old automobile-body worker, was admitted to the hospital on March 4, 1937, complaining of pain in the right shoulder and arm. He had been entirely well until 5½ months previously, when he fell, striking the back of his neck and right shoulder on a projection. He had pain in that region for 30 minutes and then resumed his work. One week later, he began to have pain in the posterior right side of the neck, right shoulder

and upper arm and a sensation of numbness in the upper arm made worse by coughing, sneezing, straining and motion and not relieved by medication, physiotherapy or strapping. A Thomas collar improved the pain, except on sneezing and coughing, for 8 weeks, when the symptoms progressed. Pain in the back of the neck, shoulder and arm became severe. Flexion, extension and lateral flexion of the neck caused numbness involving the whole arm and hand, particularly the thumb and index finger. The arm became weak and then were tremors of the muscles of the upper arm.

Examination revealed tenderness to the right of the 5th cervical vertebra and the spine of the scapula, the latter being accompanied by numbness in the arm. There was some weakness of the right arm and hypesthesia over the radial side of the forearm and the deltoid region. The reflexes of the right arm were diminished and the right ankle jerk was more active than the left. There were no pathologic reflexes. The cerebrospinal-fluid protein was 60 mg. per 100 cc. at the lumbar level and 17 mg. at the cisternal. Lipiodol examination revealed a partial block at the upper margin of the 6th cervical body. On laminectomy the 6th cervical root was found to be compressed by a ruptured disk fragment, which was removed. The patient was improved when discharged. On check-up examination and by correspondence later it was found that the patient continued to have some soreness of the right upper arm and forearm.

CASE 3 (M. G. H. 181151). J. F. B., a 38-year-old butcher, was admitted to the hospital on March 30, 1939, for pain and paresthesias in the left shoulder and arm. Five years previously he was struck by an automobile, and he grasped the radiator cap to ride the car with his knees on the bumper. There was stiffness of the neck for 4 to 5 weeks, diagnosed as strain of the cords of the left neck and shoulder. Five months previously he noticed a sensation of "pins and needles" in the left arm when he was tipped back in a barber's chair, the sensation persisting until the headrest was raised. Since then this sensation had been felt more frequently, particularly in tilting the head to the left and lying on the left shoulder. Two months later the patient began to suffer from constant tearing pain in the anterolateral region of the left upper arm and scapula. The paresthesias became almost constant, involving the radial forearm, thumb and index finger. The discomfort was aggravated by tilting the head to either side, use of the left arm and lying on the left shoulder. Some relief was obtained by raising the left arm over the head.

On examination all movements of the head against resistance and to the left without resistance produced pain over the scapula and anterolateral upper arm and paresthesias in the left radial forearm, thumb and index finger. There was some hyperalgesia over the left shoulder blade and antecubital space and hypesthesia of the left thumb. The left radial and biceps reflexes were less active than those on the right. Other reflexes were normal, and there were no pathologic reflexes. X-ray examination showed absence of cervical lordosis. Lipiodol examination was suggestive of delay in the transport of the lipiodol between the 5th and 6th cervical vertebrae on the left side. The total protein of the cerebrospinal fluid was 47 mg. per 100 cc. at the lumbar level and 25 mg. at the cisternal.

Laminectomy revealed a ruptured disk fragment compressing the 6th cervical nerve root, which was removed. The patient was symptom free after recovery from the operation, and remained so at a check-up examination two months later, at which time he was ready to go back to work.

CASE 4 (M. G. H. 397940). L. A. T., a 53-year-old farmer, entered the hospital on March 25, 1943, with complaints of pain in the neck, left shoulder and arm. Twenty years previously he fell 12 feet from a barn roof, hitting the ground with his feet down and suffering a fracture of the right knee. Six weeks before admission he slipped on the ice, wrenching his left shoulder. The pain in the left arm began 6 years previously, at first occurring only during the night. It involved the antecubital region and was associated with numbness. After the second accident both the pain and the numbness became more continuous and widespread, including the lower midcervical region and left shoulder blade and radiating over the collarbone into the deltoid region and the radial forearm. The pain, which was described as "like electricity" and "like a toothache," was made worse

turning the head to the right and by flexing it. Traction made it worse.

At examination the head was seen to be tilted to the right. Cervical spine was held rigid and was tender to pressure in its lower part. There was marked atrophy of the left biceps muscle. Motions of the left arm and hand were weak. All joints. There was hypesthesia of the lateral aspect of upper arm and the radial aspect of the forearm. The biceps, radial and abdominal reflexes were less active than those on the right. Both triceps reflexes were absent. Left knee and ankle jerks were more active than those on right, and there was a Babinski sign on the left. X-ray examination of the cervical spine revealed absence of cervical lordosis and slight tilting of the head to the right. The side of the diaphragm was elevated. Lipiodol examination showed a suggestive defect at the level of the 5th cervical interspace. The total protein of the lumbar cerebrospinal fluid was 75 mg. per 100 cc.

At operation a disk fragment compressing the left 6th cervical nerve root was found and removed. Recovery was prompt and relief was complete. The patient returned to his old job and subsequently reported, "My health is the best it has been for many years."

CASE 5 (M. G. H. 296875). J. H. O., a 43-year-old engineer, was brought to the hospital on April 8, 1941, because of weakness of both legs and arms. Twenty-three years previously he had a fall while on cavalry drill in France. Three years later he began to have "stiff necks" and pain in the left shoulder and arm, intermittently. Later on, these attacks occurred more frequently. Three weeks prior to admission he noticed a steady, sharp pain over the left shoulder blade, dorsolateral upper arm and dorsal forearm. Paresthesias in the index and middle fingers, which were aggravated by moving the spine. Because of this pain he had been unable to lie in bed for the past week. A physician recommended extraction of three teeth. When the third molar was pulled, the patient's whole body stiffened. Severe shooting pain in both hands and both feet was noted and the old shoulder and arm pain disappeared. When he tried to get out of his car at home he was unable to move his hands and feet, which felt numb. During the next few days the strength in the arms and right leg partially returned, but he was unable to pass his urine and was incontinent of feces.

Examination revealed a marked weakness of the left leg, weakness of the right leg and weakness of the grip of both hands, more so on the left side. There was anesthesia, pinprick and temperature over the right side of the body, with its upper level at the clavicle and the inner side of the right arm. There was hypesthesia to pinprick and temperature over the left chest, the left inner arm and the dorsolateral aspect of the upper arm and forearm. The arm and leg reflexes were brisk and more active on the left side than on the right. There were unsustained knee and ankle clonus, and the plantar reflexes were equivocal and possibly extensor on the left side. The bladder was paralyzed. Compression of the jugular veins produced increased numbness. A lumbar puncture showed a complete block and a total protein of 67 mg. per 100 cc. X-ray examination of the cervical spine revealed narrowing of the 5th and 6th cervical interspaces and extensive spur formation in the anterior margins of the 5th, 6th and 7th cervical vertebrae.

At operation a disk fragment was found compressing the 6th cervical root on the left side and was removed. Following the operation the patient had a complete paralysis of both legs, which gradually subsided with return of bladder and bowel function. He is able to walk and use his arms and does odd jobs, but there is still a marked pyramidal deficit.

CASE 6 (M. G. H. 392078). V. T., a 32-year-old floorman, was admitted to the hospital on February 12, 1943, for pain in the right scapular region and right arm. Sixteen years previously he had a fall, landing on his neck. There was weakness in both arms and numbness and tenderness over the anterior chest below the clavicles for 2 or 3 months. Nine years previously he suffered a concussion while playing football, with loss of consciousness for 1 or 2 hours. Two years later he noticed pain in the right scapular region, which was not affected by motions of the neck and was relieved by the extraction of teeth.

Six months prior to admission, the patient noticed pain over the upper part of the right scapula, particularly on bending the neck forward and backward. Two months later the back pain was accompanied by shooting pain in the right side of the chest, the anterolateral aspect of the upper arm, the antecubital region and the radial forearm. This pain was aggravated by sneezing and coughing. It could be relieved by extending the arm over the head. There was also a constant ache in the upper arm and forearm and tingling of the fingertips. Traction and medication were of no effect. The right arm became gradually weaker, pushing motions being chiefly affected. There were also twitchings of the biceps muscle and trembling of the hand.

Examination revealed atrophy of the right triceps and deltoid muscles, weakness on abduction at the shoulder and on extension of the forearm and fasciculations of the deltoid muscle. There were no distinct sensory disturbances. The right triceps reflex was less active than the left. Other reflexes were normal. X-ray examination of the cervical spine showed narrowing of the 6th cervical interspace. The total protein of the lumbar cerebrospinal fluid was 67 mg. per 100 cc. Lipiodol examination showed delay of transport opposite the 6th cervical interspace on the right.

At operation a disk fragment was found compressing the right 7th cervical root and was removed. The pain was instantly relieved and convalescence was uneventful. The strength and size of the affected muscles gradually became normal. The patient returned to work 3 months after the operation. At a recent check-up examination he stated, "I am lifting 20 tons of clothes each day."

CASE 7 (M. G. H. 407258). E. F., a 43-year-old mill hand, was admitted to the hospital on June 17, 1943, because of pain in the left shoulder and left arm. Six months previously while wrestling he fell against a parked car, striking his eye; three stitches were taken in the eyelid. Five weeks prior to admission he began to have severe stabbing pain involving the left shoulder blade, the dorsolateral aspect of the left upper arm and the dorsolateral aspect of the forearm on bending the head backward or turning it to the left side. The pain was associated with a tingling sensation in the dorsolateral forearm and index finger. The pain and numbness gradually became more severe and almost constant. Twitchings of the biceps muscle were also noted.

Examination showed atrophy of the left upper arm and muscle-bundle twitchings of the biceps muscle. There was marked weakness of the triceps muscles, mild weakness of the biceps muscles and some weakness of the other muscles of the forearm and hand. Hypesthesia was found over the dorsolateral aspect of the upper arm and forearm. The triceps reflex was diminished; other deep and superficial reflexes were normal. X-ray examination of the cervical spine revealed absent cervical lordosis and narrowing of the 6th cervical interspace. Lipiodol examination suggested an obstruction to the flow at a point opposite the left side of the 6th cervical interspace. The total protein of the cerebrospinal fluid was 48 mg. per 100 cc. at the lumbar level and 28 mg. at the cisternal. At operation a disk fragment was found compressing the left 7th cervical root and was removed. The postoperative course was uneventful. The patient was entirely relieved, returning to his job 4 weeks after the operation and continuing regularly since then.

CASE 8 (M. G. H. 221689). C. H. M., a 68-year-old physician, entered the hospital on November 10, 1939, with complaints of pain involving the left scapula, the ulnar side of the left arm and the little finger. Three weeks previously, while pitching horseshoes, he twisted his back and felt deep underneath the left scapula a sudden, sharp pain that radiated across the axilla down the inner upper arm, elbow and forearm into the little finger. The pain was intermittent at first, but became more constant and dull. There also was numbness in the little finger. The pain was relieved by abduction and external rotation of the upper arm with internal rotation of the forearm — by grasping the head of the bed or resting the hand under the head. The pain was increased by extension of the head.

Positive findings included tenderness of the 7th cervical spinous process, with radiation of pain down the inner arm to the little finger. The pain was reproduced by hyperextension of the head and deep pressure in the left supraclavicular

area. Extension of the forearm, adduction of the thumb, flexion of the little finger and adduction and abduction of all the fingers were slightly weak. The little finger and inner arm were a little less sensitive to pain, temperature, touch and vibration than normal. The reflexes were equal and normal with the exception of the left triceps reflex, which was extremely sluggish. No pathologic reflexes were found. X-ray examination showed mild hypertrophic changes about the margins of the lower cervical and dorsal vertebrae and diffuse osteoporosis. Lipiodol examination was inadequate owing to the patient's condition. The total protein in the lumbar spinal fluid was 103 mg per 100 cc and that in the cisternal 49 mg. Head traction was tried but was not tolerated.

At operation the left 8th cervical root was found to be compressed by a disk fragment, which was removed. Convalescence was uneventful and the pain disappeared. The patient was able to resume practice three months after the operation.

THE ROOT-COMPRESSION SYNDROME

In spite of the difference in level these cases had certain features in common. These will be analyzed

that movements such as turning and tilting the head and forward and backward bending of the neck made their discomfort worse. Other exacerbating factors were motions of the involved arm except for combined abduction and external rotation of the upper arm and internal rotation of the forearm, which were used by 3 patients to relieve the pain. Sneezing and coughing as aggravating factors were recorded in 3 cases.

Four patients complained of weakness of the arm, and 3 of them observed twitchings of some of the arm muscles.

The duration of the symptoms varied from three weeks to twenty-two years. In 4 patients it was from five to seven months.

In only 1 case did the onset of the characteristic disturbances occur at the time of the trauma. In the other patients the symptoms immediately follow-

TABLE 1. *Nature of Injury and General Symptomatology*

CASE NO.	AGE	SEX	TIME	INJURY	NATURE	IMMEDIATE SYMPTOMS	DURATION	LATE SYMPTOMS	
								NATURE	
1	37								
44		M	22 mo ago	Crank struck left arm		Pain in deltoid region for several days	11 mo	Pain, paresthesias and weakness in left arm and shoulder	
2	49	M	5½ mo ago	Struck back of neck and right shoulder on projection		Pain in right deltoid region for ½ hr	5 mo	Pain, paresthesias and weakness in right arm and shoulder, twitchings	
3	38	M	5 yr ago	Struck by car		Stiffness in neck and left shoulder for 4 to 5 wk	5 mo	Pain and paresthesias in left arm and shoulder	
4	53	M	20 yr ago	Fell 12 feet, landing with right foot on a boulder		Fracture of right knee — exacerbation of shoulder and arm pain	5 to 6 yr	Pain and paresthesias in left shoulder and arm	
			6 wk ago	Slipped on ice, wrenched left shoulder					
5	43	M	23 yr ago	Fell off horse		Apparently no ill effects	22 yr	Intermittently stiff neck, pain and paresthesias in left shoulder and arm, recently sudden paraplegia	
			3 wk ago	Forceful manipulation of neck		Paraplegia			
6	32	M	17 yr ago	Fell on neck		Arms "paralyzed" for 3 wk, numbness and tenderness over chest	6 mo	Pain, paresthesias and weakness in right arm and shoulder, twitchings	
7	43	M	6 mo ago	Fell against car while wrestling		Laceration above eye, headaches	6 wk	Pain and paresthesias in left shoulder and arm, twitchings	
8	68	M	3 wk ago	Twisted back pitching horseshoes		See case record	3 wk	Pain, paresthesias and weakness in left shoulder and arm	

first, after which the syndromes characteristic of each level will be discussed.

All the 8 patients at some time prior to the onset of their recent illness received an injury. The different types of injury, the age and sex of the patients at the time of admission, the onset and the type of symptoms are summarized in Table 1.

The ages varied from thirty-two to sixty-eight years, with an average age of forty-six years. All the patients were men. In 6 cases the left side was involved.

The symptoms that brought the patients to the hospital were pain associated with paresthesias in the region of the scapula, arm and hand. The pain was usually described as stabbing, shooting, sharp or acute. Only 3 patients complained also of pain in the lower part of the neck. In 3 others there was no history of discomfort referable to the neck. Two patients noticed pain and paresthesias in the scapular region and arm for the first time on certain movements of the neck. All patients except 1, however, stated

ing the injury were different from those experienced weeks, months or many years later. It should be mentioned, however, that the patient in Case 3 had a stiff neck for four or five weeks following the injury. It was diagnosed as strain of the cords of the left neck and shoulders. In Case 6 there was motor paralysis of both arms and paresthesias for three weeks after the patient's fall. In Case 4 the patient, who suffered two accidents, noticed an exacerbation of the symptoms after the second one.

During the course of the recent illness in any given case the type of symptoms remained about the same, but the intensity of the sensory manifestations increased and weakness, if present, became more pronounced. Only in 1 case (Case 5) did the type of symptoms change entirely, the patient becoming paralyzed during a dental operation. He was included in this series because for twenty-two years he had suffered from intermittent spells of stiffness of the neck and shooting pains in

the left shoulder and upper arm much like those experienced by the other patients.

The motor and sensory findings are summarized in Table 2. On the involved side weakness of certain muscles and diminution of arm reflexes were observed in 7 cases and atrophy and fasciculations in 4. Marked involvement of the pyramidal tracts as present in Case 5. In 3 other patients mild

changes of the lower cervical spine in 4 and absent cervical lordosis in 4. Narrowing of an interspace was always associated with hypertrophic changes. In 2 cases there was a combination of narrowing, hypertrophic changes and absent lordosis.

The different distribution of the sensory manifestations resulting from root compression at the fifth, sixth and seventh interspaces is shown in

TABLE 2. Motor and Sensory Disturbances.

CASE No	SIDE OF LESION	MOTOR DISTURBANCES					LEGS	SENSORY DISTURBANCES	
		ARM (ON SIDE OF LESION)						ARM (ON SIDE OF LESION)	OTHER PARTS OF BODY
		Atrophy	Weakness	Fibrillations	Reflexes	Weakness	Reflexes		
1	Left	Yes	Yes	Yes	Normal(?)	No	Left knee jerk more active, left plantar indefinite	Yes	No
2	Right	No	Yes	Yes	Diminished	No	Right ankle jerk more active	Yes	Possibly right side of neck and chest
3	Left	No	No	No	Diminished	No	Normal	Yes	No
4	Left	Yes	Yes	No	Diminished	No	More active on left, left Babinski	Yes	No
5	Left	No	Yes	No	More active	Yes	More active on left, plantar indefinite	Yes	Yes
6	Right	Yes	Yes	Yes	Diminished	No	Normal	No	No
7	Left	Yes	Yes	Yes	Diminished	No	Normal	Yes	No
8	Left	No	Yes	No	Diminished	No	Normal	Yes	No

unilateral pyramidal signs were found without weakness. They were on the same side as the symptoms and signs produced by the root compression in the cervical region.

Impairment of sensation in some parts of the upper extremity was recorded in 7 cases. Other parts of the body were normal except in Case 5,

Table 3. There was involvement of the scapula, the anterolateral aspect of the upper arm, the antecubital space, the radial side of the forearm and the thumb and index finger in herniations at the fifth interspace (sixth cervical root). The scapula, the dorsolateral aspect of the upper arm, the dorsal aspect of the forearm and the index and

TABLE 3. Regional Sensory Disturbances.

CASE 1 (FIFTH INTERSPACE)	CASE 2 (FIFTH INTERSPACE)	CASE 3 (FIFTH INTERSPACE)	CASE 4 (FIFTH INTERSPACE)	CASE 5 (SIXTH INTERSPACE)	CASE 6 (SIXTH INTERSPACE)	CASE 7 (SIXTH INTERSPACE)	CASE 8 (SEVENTH INTERSPACE)
Scapula (Pr, Hr)	Scapula (P)	Scapula (P, Hr)	Scapula (P)	Scapula (P)	Scapula (P)	Scapula (P)	Scapula (P)
Anterolateral upper arm (P, Pr)	Anterolateral upper arm (P, Pr, H)	Anterolateral upper arm (P)	Anterolateral upper arm (P, Pr, H)	Dorsolateral upper arm (P)	Dorsolateral upper arm (P)	Dorsolateral upper arm (P, H)	Inner upper arm (P)
Antecubital region (P, Hr)	Radial forearm (H)	Antecubital region (Hr)	Antecubital region (P, Pr)	Dorsal forearm (P)	Chest (P)	Dorsolateral forearm (P, Pr, H)	Inner forearm (P)
Forearm (P)	Thumb and index finger (Pr)	Radial forearm (Pr)	Radial forearm (P, Pr, H)	Index and middle fingers (Pr)	Dorsolateral forearm (P)	Index finger (Pr)	Little finger (P, Pr, H)
		Thumb (Pr, H)			Fingertips (Pr)		
		Index finger (Pr)					

Abbreviations: P—Pain; Pr—Paresthesias, H—Hypesthesia, Hr—Hyperesthesia

in which there was a Brown-Séquard syndrome, and Case 2, in which the disturbance was indefinite.

Tenderness of the lower cervical spine was demonstrated in 3 cases, of the scapula in 2, and of the arm muscles in 2 cases.

The examination of the lumbar cerebrospinal fluid revealed an elevated protein in 5 patients and high borderline values in the others. In only 1 case was the cisternal fluid abnormal. The dynamics were not affected except in Case 5, which had a complete block.

X-ray examination of the cervical spine showed narrowing of an interspace in 3 cases, hypertrophic

middle fingers were affected by compression of the seventh cervical root at the sixth interspace. The lesion at the seventh interspace (eighth cervical root) produced sensory abnormalities of the scapula, the inner side of the upper arm and forearm and the little finger.

There was obvious motor dysfunction of the biceps and deltoid muscles in 2 cases with compression of the sixth cervical root, and of the deltoid, biceps and triceps muscles in 2 cases with involvement of the seventh nerve root. Implication of the eighth nerve root seemed to be associated with weakness of the triceps, adductor of the thumb,

flexor of the little finger and interossei muscles.

The narrowing of the sixth interspace shown on the x-ray plates was at the sixth interspace in all 3 cases with the lesion at this level.

Lipiodol examination was done in 7 cases, with suggestive results in 4 of them.

COMMENT

The data just presented indicate that pain and disability of the shoulder and arm were the prominent symptoms in this group of patients.

The character of the pain and its association with paresthesias suggested that it was due to involvement of the nervous system. It was exacerbated by flexion, hyperextension and tilting of the neck and certain movements of the arm, and also by sneezing and coughing. It did not follow the course of any particular peripheral nerve. These features and the demonstration of the underlying pathology make it certain that the pain resulted from disease involving the sensory roots. One also may infer that the areas in which this pain and the other sensory abnormalities occurred represented the dermatomes supplied by the affected posterior roots.

With herniations at the fifth interspace, the scapula and the anterolateral aspect of the upper arm were involved in all 4 cases and the antecubital region and radial forearm in 3 cases. The site on the forearm in 1 case was not recorded. The thumb and index finger were affected in 2 cases. Figure 1 shows that this pattern follows fairly closely the arrangement of the sixth cervical dermatome as outlined by Foerster,¹³ with the exception of the radial forearm. On the chart by Pauchet and Dupret¹⁴ the sixth cervical dermatome is represented on the radial forearm.

In the second group with herniations at the sixth interspace, the scapula, dorsolateral upper arm and dorsal forearm were implicated in all cases, the index and middle fingers, and the index finger alone in 1 case each, and the fingertips in the third case. The scapular pain, which was definite, could not be explained by using Foerster's outline. In Pauchet and Dupret's outline the seventh cervical dermatome is represented in this area. In both figures the seventh cervical dermatome does not include the dorsolateral aspect of the upper arm.

The only patient in this group who had a herniation at the seventh interspace presented sensory manifestations in accordance with the outline of Pauchet and Dupret, including the shoulder blade, the inner, upper and lower arm and the little finger.

The distribution of the sensory phenomena in the upper arm and forearm and shoulder appeared to be consistent and characteristic for each root. The pattern of the sensory manifestations of the fingers was not uniform. In 2 cases with involvement of the sixth cervical root the fingers remained free. The index finger, which Semmes and Murphey¹² believe is almost entirely innervated by the seventh

cervical root, and the thumb were affected in the other 2 cases. Compression of the seventh cervical root produced manifestations in the index finger, both in the index and middle finger, and on the fingertips. These differences were probably due to variations of the dermatome distribution, which are known to occur particularly in the fingers.^{12, 14}

The question may also be raised whether involvement of the scapula, observed in all the patients

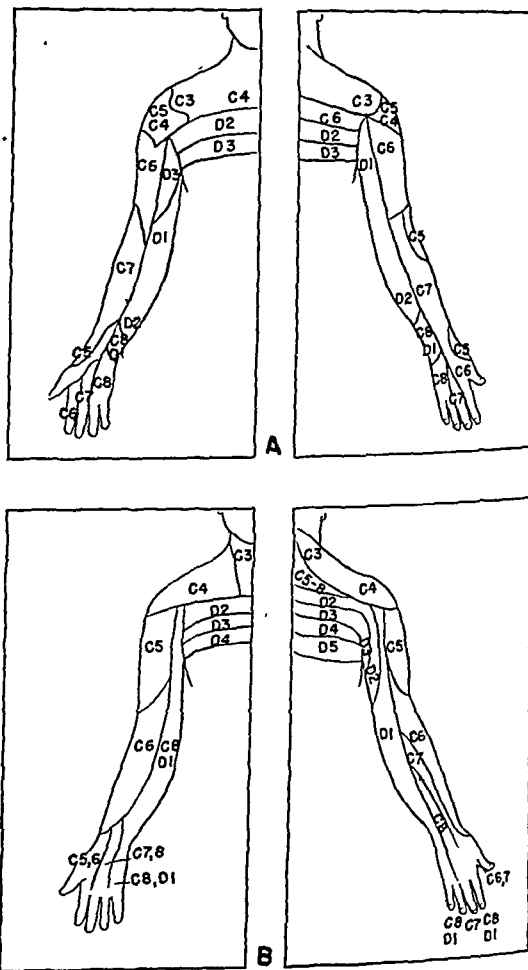


FIGURE 1. Distribution of Cervical Dermatomes. The upper drawings (A) are according to Foerster,¹³ and the lower (B) according to Pauchet and Dupret.¹⁴

regardless of the level, is due to an overlap phenomenon or a true representation of the affected roots in this area. Study of a larger number of cervical-disk cases will be necessary for a better understanding of all these problems, and perhaps of the extent of cervical dermatomes in general. The different outlines found in the textbooks are extremely confusing.

Semmes and Murphey did not describe the distribution of the arm pain in their patients with herniation of the sixth interspace. Their findings with reference to the index and middle fingers and

shoulder are in agreement with ours. The question of heart disease as the underlying pathology did not come up in these cases. Only 1 patient experienced pain over the chest, but he had a right-sided lesion. The absence of neck pain in 5 of 8 patients is worth emphasizing.

As to the motor dysfunction, diminution of reflexes of the involved arm were usually present without significant difference of the biceps, triceps, and radial reflexes at different levels of the herniation.

Weakness, atrophy and twitchings of the biceps and deltoid muscles were recorded in lesions at the fifth interspace, of the deltoid, biceps and triceps muscles at the sixth, and of the triceps, adductor pollicis, flexor digiti quinti and interossei muscles at the seventh. The records, however, were not too clear with reference to the analysis of the motor disability, perhaps because pain interfered with a systematic examination. A more detailed examination and the use of chronaxie determinations and electromyograms in the future may be of some value for a better definition of the motor changes. The number of the muscles affected by involvement of the respective anterior roots should be greater than have been observed if the present knowledge of the motor segmental innervation is correct.

With the exception of Case 5, which can be omitted from the discussion, symptoms of the long tracts of the spinal cord were absent. The dynamics of the cerebrospinal fluid were normal, and although mild or equivocal pyramidal signs were recorded in 4 cases, the basic clinical picture in all 7 cases was not due to cord compression.

X-ray changes of diagnostic value comprised absent cervical lordosis and narrowing of the sixth cervical interspace. The latter was found in all 3 cases with herniation at this level. Semmes and Murphey found loss of the cervical curve in 2 cases but no narrowing of the disk. The cerebrospinal fluid examination was useful when the total protein was elevated. In 2 of the cases with a doubtful value, x-ray changes and other evidence led to a lipiodol examination, which suggested the presence of the lesion.

The lipiodol findings were negative in only 1 case; in 2 cases it could not be moved from the site of the injection, and in 4 cases there was a delay of the passage of the oil at the level of the protruded disk. In the more recent cases the oil was removed after the examination at the lumbar level, as suggested by Kubik and Hampton.⁴

DIFFERENTIAL DIAGNOSIS

When a patient presents himself with ordinary complaints of pain in the shoulder and arm, the discovery of the true seat of the disease may be beset with difficulties. Arthritis of the spine and shoulder, bursitis, brachial neuralgia and neuritis, cervical rib, elongated transverse processes of the

seventh cervical vertebra and more recently scalenus anticus syndrome are popular diagnoses. Semmes and Murphey¹² emphasized the similarity of their syndromes and coronary disease. One might as well also include gall-bladder disease if the herniation is on the right side, pleurisy and tumors of the apex of the lung. Some of these syndromes are vaguely defined clinically as well as pathologically and their separation from each other is not always possible. The addition of a new entity to this long list seems to complicate things even more, but actually it may simplify the problem. Undoubtedly a fair number of cases formerly treated under one of the customary diagnoses will be interpreted and handled more rationally if the picture of cervical-root compression by a disk fragment becomes better known.

It is beyond the scope of this paper to discuss seemingly similar symptoms and signs of the aforementioned entities and the syndrome of a ruptured disk. Usually a good history with careful evaluation of the complaints shows the specific nature of the symptoms. As pointed out before, root pain has certain characteristics. If it is not recognized as such by its quality and distribution, its onset and course and the factors that aggravate or relieve it may be suggestive. Acromial bursitis, for instance, interferes with the abduction and outward rotation of the upper arm, which is very painful. Several of these patients volunteered the information that this particular movement relieved their pain. The mechanical irritation by a cervical rib or tight scalenus anticus muscle is lessened by tilting the head to the affected side; the reverse was true in these cases.

Regardless of whether the complaints of the patient can be properly evaluated, a systematic neurologic examination, including lumbar puncture and possibly lipiodol studies, is indicated, if other measures fail to disclose some definite underlying lesion. Occasionally a lumbar puncture alone or the combination of an absent cervical lordosis and narrowing of an interspace decides the issue, but it is not one symptom or sign that characterizes a clinical entity. A satisfactory diagnosis is based on collateral evidence.

Table 4 shows the more important findings in 7 cases.* Every one of these patients showed a combination of signs that is not compatible with extraspinal disease. The syndrome was that of intraspinal disease, unlike that of a tumor or syringomyelia, not to mention other less relevant possibilities.

TREATMENT

All patients had various forms of treatment prior to their hospital admission, without permanent relief. Such measures comprised baking and massage,

*Case 5 was omitted because of obvious cord compression on admission.

lamp treatments, strapping and head traction. One patient was injected locally with novocain. The laminectomy and removal of the disk fragment produced good results in 6 cases. In 1 case the improvement was not too impressive. In one of the early cases in which the disk fragment could

In the recent cases the operation consisted of subtotal hemilaminectomy. Small pieces of bone were removed from the adjacent lamina on one side. A lateral opening in the dura was made and only the nerve roots were exposed. After gentle retraction of the roots the disk was removed transdurally.

TABLE 4. Summary of Data

CASE 1	CASE 2	CASE 3	CASE 4	CASE 6	CASE 7	CASE 8
Left root pain increased by certain movements of left arm, paresthesias	Right root pain increased by certain movements of neck and right arm, sneezing and coughing, paresthesias	Left root pain increased by certain movements of neck and left arm, paresthesias	Left root pain increased by certain movements of neck and left arm, paresthesias	Right root pain increased by certain movements of neck and right arm, sneezing and coughing, paresthesias	Left root pain increased by certain movements of neck and possibly left arm, sneezing and coughing, paresthesias	Left root pain increased by certain movements of neck and left arm, paresthesias
Left segmental sensory disturbances	Right segmental sensory disturbances	Left segmental sensory disturbances	Left segmental sensory disturbances	Right arm atrophy, weakness, fibrillations, right arm reflexes diminished	Left segmental sensory disturbances	Left segmental sensory disturbances
Left arm atrophy, weakness, fibrillations	Right arm weakness, fibrillations, right arm reflexes diminished	Left diminished arm reflexes	Left arm atrophy, weakness, left arm reflexes diminished	Narrowing of 6th cervical interspace, absent cervical lordosis	Left arm atrophy, weakness, fibrillations, left arm reflexes diminished	Left arm weakness, left arm reflexes diminished
Left knee jerk increased, indefinite plantar	Right ankle jerk increased	Absent cervical lordosis	Left leg reflexes increased, left Babinski		Narrowing of 6th cervical interspace, absent cervical lordosis	
			Absent cervical lordosis			
Total protein 43 mg per 100 cc	Total protein 60 mg per 100 cc, partial lipiodol block	Total protein 47 mg per 100 cc, partial lipiodol block	Total protein 75 mg per 100 cc, partial lipiodol block	Total protein 67 mg per 100 cc, partial lipiodol block	Total protein 48 mg per 100 cc, partial lipiodol block	Total protein 123 mg per 100 cc

not be removed for technical reasons, the pain was relieved but the motor disability persisted. In Case 5, with recent cord compression, gradual improvement of the motor and sensory functions of the long

Figure 2 shows the approximate location of the disk fragment as compared with the fragments in Stookey's group producing cord compression.

All the operations in this series were performed under general anesthesia. Consequently we have no experience with the determination of the level of the lesion by pressure on the yellow ligament and subsequent novocain injection, as suggested by Semmes and Murphey. Their procedure may be the method of choice in cases suitable for local anesthesia.

SUMMARY AND CONCLUSIONS

Eight cases of herniation of the nucleus pulposus in the lower cervical spine are reported. There were lesions at the fifth cervical interspace in 4 cases, at the sixth in 3 and at the seventh in 1, with involvement of the sixth, seventh and eighth cervical roots, respectively.

The clinical data were brought together in a syndrome that comprised root pain and local sensory and motor disturbances, as well as positive x-ray, cerebrospinal-fluid and lipiodol findings.

The distribution of the sensory abnormalities was compared with standard dermatome charts. In these cases the sixth cervical dermatome seemed to involve the scapula, the anterolateral aspect of the upper arm, the antecubital space, the radial forearm and its thumb and index finger. The seventh cervical dermatome seemed to involve the scapula.

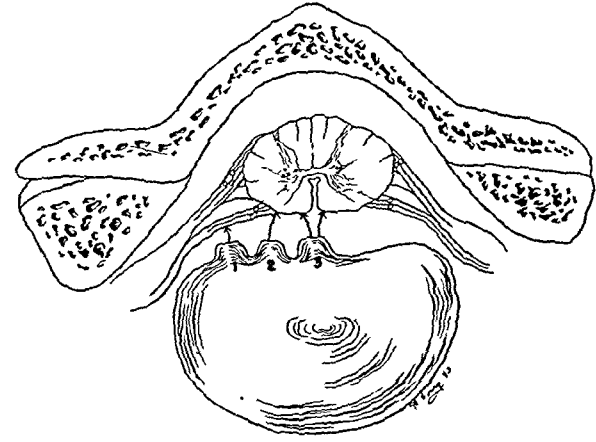


FIGURE 2. Diagram Showing Various Types of Herniation of the Cervical Disk.

The three types are as follows. 1—herniation producing cord compression; 2—herniation producing unilateral compression of the ventral root (Stookey's Group II); and 3—herniation producing bilateral compression of the ventral roots (Stookey's Group I).

tracts and roots took place. The other patients were relieved of their pain dramatically. The recovery of muscle function, if impaired, was gratifying.

the posterolateral aspect of the upper arm, and the dorsal surface of the forearm and the index and middle fingers. The eighth cervical dermatome seemed to involve the scapula, the inner and upper arm, the forearm and the little finger.

The importance of a systematic neurologic examination in cases with pain or disability of shoulder and arm is emphasized, to separate the apparently specific syndrome of cervical herniations of the nucleus pulposus from other extraspinal and intraspinal entities.

The results of the removal of the disk fragments by laminectomy — more recently by subtotal hemilaminectomy — were good.

The clinical data of 3 cases included in this paper were obtained through the courtesy of Drs J. S. Hodgson, T. J. Putnam and J. C. White.

319 Longwood Avenue

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SEROLOGIC TYPES OF HEMOLYTIC STREPTOCOCCI ISOLATED FROM SCARLET FEVER IN MASSACHUSETTS, 1942-1943*

LIEUTENANT S. M. WHEELER (MC), U.S.N.R.† AND G. E. FOLEY‡

BOSTON

DURING 1942 and 1943, hemolytic streptococci isolated from the throat swabs of patients with scarlet fever admitted to various Massachusetts hospitals were classified as to serologic type. The laboratory studies were carried out at the Department of Preventive Medicine, Harvard Medical School,§ and arrangements for the provision of throat cultures were made possible through the cooperation of the Division of Communicable Diseases of the Massachusetts Department of Public Health.¶

In this period a total of 631 throat swabs were examined, of which 427 (67.7 per cent) were positive for Group A hemolytic streptococci. The low percentage of positive cultures from scarlet-fever cases can be explained in part by the loss of viability of organisms sent through the mail. These strains were

classified as to serologic type by the method of Griffith.¹ Slide agglutination was facilitated by the digestion of granular or self-agglutinating cultures by the tryptic digest method described by Allison.²

The serologic types of hemolytic streptococci isolated from scarlet-fever cases in different localities are presented in Table 1. The similarity of the predominant types of streptococci causing this disease in these various localities is noteworthy. In Table 2 the most frequent scarlet-fever types in two earlier Boston studies are compared with those encountered in the Massachusetts communities in 1942 and 1943, which are represented by community in Table 1. It is not possible to draw conclusions from these data concerning the limits of constancy of the streptococcus-type pattern in scarlet fever, but the emergence of certain predominant types and the tendency of others to decline or disappear can be seen.

The available data suggest that during the period of seasonal prevalence of streptococcal infection certain types maintain themselves as the cause of scarlet fever in a large proportion of cases. From these studies it is obvious that in Massachusetts the type pattern in scarlet fever varies from year to year. Further observations are necessary to determine the number of years that single types continue to occur predominantly in scarlet fever. There is a suggestion that Type 2 has maintained

*From the Department of Preventive Medicine, Harvard Medical School.

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‡Formerly, research associate, House of Good Samaritan.

§Technical associate, Department of Preventive Medicine, Harvard Medical School; bacteriologist, House of Good Samaritan.

¶We limit the limits of laboratory facilities, it is possible for this laboratory to type hemolytic streptococci from scarlet fever and other infections occurring in the New England area. Swabs or cultures submitted should be accompanied by the patient's name and address, age, sex, date of onset of disease, date of culture, source of swab or culture and diagnosis and treatment (if any), together with the sender's name and address so that the results may be reported.

We are indebted to Dr. R. F. Feemster, director of the Division of Communicable Diseases, Massachusetts Department of Public Health, for making arrangements to carry on this study.

itself as a major cause of the disease during the months of high seasonal prevalence in both 1942 and 1943.

Evidence has accumulated in the literature that all the thirty or more well-established types have been found in scarlet fever. This is borne out by laboratory studies indicating that the common erythrogenic toxin, the so-called "N.Y.-5," is broadly valent over various serologic types in Group A

an infection without rash from a case of scarlet fever and in turn transmit the infection to contacts in whom illness manifests itself in a rash only if they have a low immunity to the Dick toxin.

This variety of clinical manifestation is best observed in milk-borne or food-borne outbreaks of streptococcal infections caused by one strain or type infecting from a common source. The work of Stebbins, Ingraham and Reed⁸ and of Dublin et al⁹

TABLE 1. *Predominant Types of Hemolytic Streptococci in Scarlet Fever in Massachusetts Cities*

COMMUNITY	YEAR	NO. OF POSITIVE CULTURES	PREDOMINANT TYPES			PERCENTAGE OF PREDOMINANT TYPES
			FIRST	SECOND	THIRD	
Boston	1942	19	2	19*	8	90
Worcester	1942	34	2	19*	8	80
Springfield	1942	6	19*	25	8	100
Fall River	1942	6	2	—	—	100
Norfolk	1942	5	2	—	—	100
Boston	1943	7	2	19*	—	100
Worcester	1943	351	2	1	8	71

*Weak cross reaction with Types 4, 24, 26 and 29

and certain Group C strains of hemolytic streptococci.⁵ The quality of toxigenicity is apparently a characteristic easily acquired or lost. Although the circumstances that favor the production of erythrogenic toxin by a given strain are not yet known, epidemiologic observations suggest that types vary in their production of toxin from time

on milk-borne sore throat and scarlet fever reveals the importance of the antitoxic immunity of the host in determining the presence or absence of a rash in the resulting infection. Secondary cases in the same household may also show these characteristics. Table 3 shows the types of hemolytic streptococci isolated from multiple cases in the same family in

TABLE 2. *Percentage Distribution of Predominant Types of Hemolytic Streptococci Isolated from Scarlet Fever in Massachusetts.*

STUDY	YEAR	NO. OF CASES TYPED	PREDOMINANT TYPES			PERCENTAGE OF PREDOMINANT TYPES
			FIRST	SECOND	THIRD	
Boston ³	1938-1939	340	15 (45%)	13 (4%)	11 (3%)	51.5
Boston ⁴	1939-1940	35	2 (55%)	6 (11%)	—	66.4
Massachusetts	1942	69	2 (57%)	19* (22%)	8 (6%)	85.6
Massachusetts	1943	358	2 (26%)	1 (26%)	8 (18%)	69.8

*Weak cross reaction with Types 4, 24, 26 and 29

to time and from place to place. The appearance of predominant type patterns suggests that locally and temporally certain types are the most successful rash producers. The streptococcus types predominant in scarlet fever can be compared in epidemiologic behavior with the pneumococcus types most frequently associated with pneumonia.

A type study of scarlet-fever streptococcus strains in regions such as Massachusetts reveals that in addition to the predominant types, a variety of other strains are at times found in the admission cultures of patients. This serves to emphasize the essential unity of scarlet fever with other streptococcal infections. The appearance of a rash in a person with hemolytic streptococcus infection depends on the toxigenicity of the organism, a property that is present in varying degree in many types, and susceptibility of the host to this toxin, as indicated by the positive Dick test. As Gordon^{6,7} has pointed out, a Dick-negative subject may contract

this study. Infections without rash did not appear with scarlet-fever infections in this series. The cultures were submitted from contagious-disease hospi-

TABLE 3. *Serologic Types of Hemolytic Streptococci from Multiple Cases of Scarlet Fever and Other Infections in Thirty-six Families.*

SEROLOGIC TYPE IN MULTIPLE CASES	NO. OF PRIMARY AND CO-PRIMARY, CASES	NO. OF SECONDARY CASES FROM HOUSEHOLD EXPOSURE
2	14*	19†
1	11	10
8	7	11
6	6	3
19	3‡	1
5	2	1
15	1	1

*Includes cases in one family diagnosed as septic sore throat

†A case of abscessed finger secondary to a case of scarlet fever

‡Includes 2 primary cases of streptococcal meningitis

tals, which are apt to admit patients with streptococcal infection only if a rash is present, in accordance with the usual public-health administrative

cedures. Undoubtedly a periphery of persons with nonscarlatinal infection was associated with these hospitalized family cases but were themselves not admitted to the hospital. The consistency of type in the infecting organisms from secondary cases in the same household, as shown in Table 3, seems to confirm that these secondary cases are the result of true household exposure.

The study of the distribution of streptococcus types in scarlet fever raises the question of the relation of the type pattern to the epidemiologic and clinical features of the disease. Relatively few data

Balkan countries scarlet fever was in an epidemic phase in which Type 10 was a highly effective invader and rash producer. In England, the disease may be more in an endemic or perhaps interepidemic phase, with four effective strains, Types 1, 2, 3 and 4, causing most of the disease, yet with no one of these types acting as a truly epidemic strain on a wide scale. Patterns differ in other countries, and in North America the typing evidence suggests a sporadic appearance of predominant scarlet fever types. It may be that the relative mildness of the disease in recent years in this country is reflected in the variety

TABLE 4. *Percentage Distribution of Predominant Types of Hemolytic Streptococci in Scarlet Fever in the United States and Canada.*

STUDY	YEAR	No. OF CASES TYPED	PREDOMINANT TYPES					PERCENTAGE OF PREDOMINANT TYPES	
			FIRST	SECOND	THIRD				
<i>Community surveys:</i>									
Binghamton, N. Y. ¹³	1939-1940	21	19*	(53%)	6	(10%)	—	—	63
Baltimore, Md. ¹³	1937-1938	105	3	(22%)	4	(13%)	2	(10%)	45
Baltimore, Md. ¹⁴	1940	39	19	(15%)	8	(15%)	6	(15%)	45
Chicago, Ill. ¹⁵	1934-1935	243	3	(25%)	6	(22%)	2	(21%)	68
New Haven, Conn. ¹⁶	1940-1941	11	3	(100%)	—	—	—	—	100
San Francisco, Cal. ¹⁷	1941	15	11	(40%)	25	(27%)	—	—	67
Toronto, Canada ¹⁸	1940-1941	88	1	(21%)	2	(19%)	3	(19%)	59
Halifax, Canada ¹⁹	1941	57	19†	(37%)	30	(26%)	3	(12%)	75
Ottawa, Canada ²⁰	1940-1942	907	3	(56%)	19†	(12%)	4	(8%)	76
New Haven, Conn. ²¹	1943	3	14	(100%)	—	—	—	—	—
<i>Multiborne and food-borne outbreaks:</i>									
Massachusetts ^{22, 23}	1942	9	2	(100%)	—	—	—	—	100
New York State ²⁴ :									
Wellsville	1936	?	3	—	—	—	—	—	—
Owego	1936	?	15†	—	—	—	—	—	—
Pultney	1941	4	3	(100%)	—	—	—	—	100
Cannonsville	1942	?	3	—	—	—	—	—	—
<i>Military surveys:</i>									
New England area (military training camp) ¹³	1941	36	1‡	(67%)	17	(8%)	8	(8%)	83
Illinois area ²⁵	1941-1942	23	26	(40%)	18	(26%)	14	(26%)	92
	1942	2	11	(100%)	—	—	—	—	—
Kentucky area ²⁵	1942	8	17	(50%)	4	(25%)	24	(13%)	88
Wyoming area ²⁵	1942	45	19	(89%)	11	(5%)	15	(2%)	96
Western area ²⁶	1943	75§	19	(100%)	—	—	—	—	—
Middle-western area ²⁷	1943	95	3	(36%)	19	(33%)	17	(15%)	84
Canada (military recruits) ²⁸	1940-1942	50	19†	(52%)	3	(18%)	6	(16%)	86
New York (naval recruits) ²⁸	1942	72	19	(98%)	—	—	—	—	98
Maryland (naval recruits) ²⁹	1943	38	3	(55%)	19	(37%)	1	(5%)	97

*Weak cross reaction with Types 4, 24, 26 and 29.
†Cross reactions with Types 17 and 23.
‡Weak cross reaction with Type 1.
§Approximate; all cases same type.

are available from North America on streptococcus typing. Table 4 gives the available information on scarlet-fever types from the literature and from unpublished work in the United States and Canada. These data may be compared with those from Great Britain, where extensive study carried on since 1926 shows that Types 1, 2, 3 and 4 cause at least half the cases of scarlet fever but vary from year to year in their relative frequency.^{10, 11} Studies over a period of five years in Rumania and other eastern European countries show that the most constant high percentage of scarlet fever is caused by Type 10, although there are fluctuations in relative preponderance.¹² It may be that during these years in the

of types associated here with scarlet fever. On the other hand, the emergence of a single type associated with a high percentage of cases may be an indication of scarlet fever in a severe epidemic form.

The geographic limits of a type pattern in scarlet fever are yet to be defined. There is some suggestion from Table 4 that the patterns are fairly widespread. Other studies on throat cultures in normal population groups show similarities of streptococcus-type patterns that fluctuate only in relatively large units of time and space.²⁷

Circumscribed outbreaks such as occur in institutions or from such accidents of environmental sanitation as the contamination of raw milk may not

itself as a major cause of the disease during the months of high seasonal prevalence in both 1942 and 1943.

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Boston ³	1938-1939	340	15	(45%)	13	(4%)	11	(3%)	51.5
Boston ⁴	1939-1940	35	2	(55%)	6	(11%)	—	—	66.4
Massachusetts	1942	69	2	(57%)	19*	(22%)	8	(6%)	85.6
Massachusetts	1943	358	2	(26%)	1	(26%)	8	(18%)	69.8

*Weak cross reaction with Types 4, 24, 26 and 29.

to time and from place to place. The appearance of predominant type patterns suggests that locally and temporally certain types are the most successful rash producers. The streptococcus types predominant in scarlet fever can be compared in epidemiologic behavior with the pneumococcus types most frequently associated with pneumonia.

A type study of scarlet-fever streptococcus strains in regions such as Massachusetts reveals that in addition to the predominant types, a variety of other strains are at times found in the admission cultures of patients. This serves to emphasize the essential unity of scarlet fever with other streptococcal infections. The appearance of a rash in a person with hemolytic streptococcus infection depends on the toxigenicity of the organism, a property that is present in varying degree in many types, and susceptibility of the host to this toxin, as indicated by the positive Dick test. As Gordon^{6,7} has pointed out, a Dick-negative subject may contract

this study. Infections without rash did not appear with scarlet-fever infections in this series. The cultures were submitted from contagious-disease hospi-

TABLE 3. Serologic Types of Hemolytic Streptococci from Multiple Cases of Scarlet Fever and Other Infections in Thirty-six Families.

SEROLOGIC TYPE IN MULTIPLE CASES	NO OF PRIMARY AND CO-PRIMARY, CASES	NO OF SECONDARY CASES FROM HOUSEHOLD EXPOSURE
2	14*	19†
1	11	10
8	7	11
6	6	3
19	3‡	1
5	2	1
15	1	1

*Includes cases in one family diagnosed as septic sore throat.
†A case of abscessed finger secondary to a case of scarlet fever.
‡Includes 2 primary cases of streptococcal meningitis.

tals, which are apt to admit patients with streptococcal infection only if a rash is present, in accordance with the usual public-health administrative

POLYARTHRITIS IN SICKLE-CELL ANEMIA*

H. G. BRUGSCH, M.D.,† AND DOROTHY GILL, M.D.‡

BOSTON

SICKLE-CELL anemia has long been known to simulate rheumatic fever. Huck¹ was the first to describe cardiovascular involvement in this form of anemia, and King and Janeway² have emphasized electrocardiographic changes similar to those found in rheumatic fever, such as prolongation of the PR interval. Klinefelter,³ in a summary of the present knowledge of the heart in sickle-cell anemia, noted at autopsy the absence of valvular disease in patients who had died of sickle-cell anemia and heart failure. Although on the whole little attention has been paid the heart pathologically, mention has been made of myocardial scars, flabbiness of the muscle and enlargement of the right ventricle (Bauer⁴).

Despite the fact that the high incidence of combined cardiovascular disease, joint pain and fever in sickle-cell anemia is stressed in publications from the South (Wintrobe⁵ and Bauer⁴), the frequent occurrence of these symptoms in Negroes living in the northern states has attracted scant attention. Because of the prevalence of true rheumatic fever in Whites as well as in Negroes in the North, the diagnosis of rheumatic fever is always uppermost in the mind of the physician when a young Negro complains of joint pains in a febrile disease of unknown etiology. This is particularly regrettable since sickle-cell anemia, once considered, can be easily demonstrated by a sealed wet preparation of the blood. In 3 of the 4 cases reported herein the correct diagnosis was missed because such preparations were not made. Wet preparations should, therefore, be included in the examination of any Negro with symptoms suggesting rheumatic fever, regardless of the presence or absence of anemia. In one of the patients (Case 3), sickle-cell anemia was considered and wet preparations were studied. When sickling did not occur after twenty-four hours, the diagnosis was abandoned. Further studies revealed that in this case the tendency to sickle did not appear until forty-eight hours had elapsed, and it was later found necessary to observe these preparations for at least ninety-six hours.

The following is a summary of 4 cases of sickle-cell anemia found among 16 Negroes whose illness had been erroneously diagnosed as active or inactive rheumatic fever.

CASE REPORTS

CASE 1. T. L., a 12-year-old Negress, at the age of 5 began to have prolonged episodes of low-grade fever, frequently associated with shorter periods of pain in the muscles and joints. At other times she had vague abdominal pain. In

July, 1941, when such an episode was observed by the district physician, a diagnosis of rheumatic fever was made. After 1 month of bed rest an inconstant, soft systolic murmur was heard at both apex and base. The patient returned to school 5 months later and was seen regularly in the Out-patient Department, where a wet preparation of the blood showed sickling after 96 hours. Some weeks later, the sickling was found to be immediate. The heart was normal by x-ray. The electrocardiogram showed sinus arrhythmia, with P₁ and P₂ upright, P₃ inverted, a PR interval of 0.12 second, a QRS complex of 0.06 second, T₁ upright and T₂ inverted, thus being within normal limits for this age. The lowest hemoglobin found was 67 per cent, the lowest red-cell count 3,570,000 and the white-cell count 6500. The blood sedimentation rate was normal.

CASE 2. J. H., a 12-year-old Negress, at the age of 7 was found to have a cardiac murmur. At times she had pain in the thighs. Intermittent icterus of the scleras, not associated with other signs of illness, had been observed by the mother since the age of 9. In 1939, the patient was hospitalized because of an attack of acute abdominal pain, considered by her physician to be caused either by appendicitis or by rheumatic fever. A blood test, however, showed sickling, and a diagnosis of sickle-cell anemia was made. Thereafter the patient was not again under medical observation until March, 1942, when she was examined for acute pharyngitis. A rough apical systolic murmur was heard at that time. A wet preparation of the blood showed marked sickling. The blood sedimentation rate was normal (3.5 mm. per hour). X-ray examination of the chest showed the heart to be definitely enlarged to the left. The electrocardiogram read as follows: P and T upright, Q 3 mm., QRS complex normal, PR interval 0.18 second and Lead 4 normal. The hemoglobin was 57 per cent, the red-cell count 2,700,000, and the white-cell count 15,000, with 46 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 13 per cent monocytes, 18 per cent eosinophils, and 1 per cent basophils. The icteric index was 25.

CASE 3. B. M., a 27-year-old Negress, enjoyed fairly good health until the age of 25, when she suddenly developed fatigue, dyspnea on exertion and dizziness. Because of a history of "rheumatism" 10 years before, a blood pressure of 155/105 and a short, rough apical systolic murmur, a diagnosis of rheumatic heart disease was made. Anemia was present at that time, — the red-cell count was 4,550,000 and the hemoglobin 55 per cent — but was attributed to a persistent menorrhagia. A blood Hinton test was negative, although 4 years previously the patient had contracted syphilis and had received 12 months' treatment. Ferrous sulfate caused moderate improvement, both symptomatically and in the blood picture. The patient ceased coming to the clinic after 4 months. On readmission 1 year later, hypochromic anemia and hypertension were again present. A wet preparation of the blood showed sickling. The hemoglobin was 50 per cent, the red-cell count 4,080,000, and the blood sedimentation rate 20 mm. per hour. An electrocardiogram showed sinus rhythm with ventricular extrasystoles. P₁ was flat. P₂ and P₃ upright, T₁ flat, T₂ and T₃ low, and R₄ inverted; the PR interval was 0.20 second, and the QRS complex 0.06 second. This was considered suggestive of myocardial damage. X-ray examination showed a normal outline of the heart.

CASE 4. L. D., a 28-year-old Negress, was first seen because of headaches of long standing. She stated that she had had two episodes of moderate joint pain without swelling 3 and 10 years previously, but did not recall whether fever had been present. Physical examination revealed a normally developed girl with definite pallor but no jaundice of the mucous membranes. The joints were normal. There was dyspnea on moderate exertion, and at the apex there was a loud Grade II systolic murmur, transmitted to the axilla. The heart was not enlarged either by percussion or x-ray; the rhythm was regular and the blood pressure 110/60. A

*From the Arthritis Clinic and the District Service of the Boston Dispensary, New England Medical Center.

†Instructor in medicine, Tufts College Medical School, and physician, Boston Dispensary (on leave of absence).

‡Formerly, district physician, Boston Dispensary.

always be caused by the prevailing types in the community. In the same way, closely herded communities, such as Army and Navy training stations may show predominating types different from those of the surrounding population. Such differences between military and civilian types may have epidemiologic importance at the present time. If the semi-isolated military community finds scarlet fever and streptococcal disease caused by the same types as in the surrounding population, the problem of control is shared with those outside. If the streptococcus-type flora is indigenous to the camp, the indications for control lie in the environment within the compound.

SUMMARY

Types of hemolytic streptococci associated with scarlet fever in certain Massachusetts cities during 1942 and 1943 were predominantly Types 2, 1, 8 and 19 in that order of frequency. During this period there was some shifting of type in relative order of frequency among the predominant types, although Type 2 maintained itself as a major cause of scarlet fever.

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MEDICAL PROGRESS

RECENT ADVANCES IN SURGERY (Concluded)*

ALFRED BLALOCK, M.D.†

BALTIMORE

HYPERPARATHYROIDISM

THE first successful operation for removal of a parathyroid tumor was performed by Landl,³⁴ of Vienna, in 1925. This patient had von Recklinghausen's disease, and improvement in the condition of the bones followed. This observation was instrumental in altering the previously held concept that the parathyroid enlargement was secondary to the disease of the bones. The view was then held for several years that the parathyroid hormone acted primarily on bone and that any significant disorder of hormone production must result in changes in the bones. Following the preparation of parathyroid extract by Collip, the pathologic physiology of hyperparathyroidism could be approached and was clarified. The working out of the clinical picture was done at the Massachusetts General Hospital by Albright, Aub, Bauer and others, and the frequent association of urinary calculi with hyperparathyroidism was noted and studied. These and other observations led to the establishment of the fact that the disorder in hyperparathyroidism is primarily one of metabolism.

As a result of careful diagnostic studies by the medical staff and of the excellent procedures devised by Churchill and Cope for identification and removal of abnormalities of the parathyroid glands, 67 patients³⁵ with a proved diagnosis of hyperparathyroidism were operated on at the Massachusetts General Hospital in the years 1932 to 1942. The majority of these patients had renal calculi and no demonstrable disease of bone. As to the frequency of hyperparathyroidism in association with renal stones, the following statement of Cope³⁶ is of interest:

Both Fuller Albright and I are agreed in the impression that approximately 15 per cent of patients with renal stones in this part of our world have hyperparathyroidism as the cause of these stones. In only a few of these cases is the disease so marked that it can be picked up either by presence of bone disease or by one blood examination. Persistent effort and care are necessary to weed out the patients with hyperparathyroidism. A number of blood examinations have to be made and the patient is often followed for quite a while before the diagnosis is finally established.

The surgical treatment of this disorder will not be discussed in detail, but it is well to emphasize the fact that the problem is concerned with the site

as well as the size of the tumor or hyperplasia. The parathyroid glands, whether adenomatous, hyperplastic or uninvolved, have been found in various locations between the larynx and the heart. In approximately 20 per cent of the cases at the Massachusetts General Hospital the adenoma has been in the anterior or posterior mediastinum. The procedure recommended by Cope³⁷ is as follows: At the first stage the neck and the posterior mediastinum are explored through a supraclavicular incision. If the offending gland or glands are not found, the anterior mediastinum is explored through a median sternotomy at another operation. It is well to remember that all the glands may be hyperplastic. Visualization of the parathyroid glands in such cases should be followed by total removal of three and subtotal resection of the fourth. The finding of one adenoma does not mean that others may not be present. It is desirable whenever possible to locate all the glands.

The mortality rate with this operation has been low and the results in general have been excellent. Cope³⁶ states that there has been no further formation of stones in the urinary tract in patients with corrected metabolism. In patients with lesions of bones, a thick wall of bone is deposited around the cyst so that the bone is strengthened but the cyst does not disappear. In addition, several patients with severe anemia have shown decided improvement. The development of this entire subject represents a brilliant accomplishment, particularly on the part of the staff of the Massachusetts General Hospital.

THE THYMUS GLAND AND MYASTHENIA GRAVIS

Nothing is known about the function of the thymus gland and little about the pathogenesis of myasthenia gravis. It is known that a significant percentage of patients with myasthenia gravis have been found by roentgenography, operation or autopsy to have a tumor of the thymic region. The lesion is usually benign, and is rare in patients who do not have myasthenia gravis.

The results that followed the removal of benign thymomas from patients with myasthenia gravis encouraged Harvey, Ford, Lilienthal and myself³⁸ in July, 1941, to determine the effect of total thymectomy without regard to the presence or absence of a tumor. This was the first time that the effect of total removal had been studied in man. Since July, 1941, we have removed the thymus gland

*From the Department of Surgery, Johns Hopkins University and Hospital.

†The Shattuck Lecture, delivered at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

†Surgeon-in-chief, Johns Hopkins Hospital; professor of surgery, Johns Hopkins University School of Medicine.

few rales were present over both lung bases. The hemoglobin was 65 per cent, and the red-cell count 3,560,000, and the white-cell count 15,000, with 58 per cent polymorphonuclear leukocytes, 25 per cent lymphocytes, 14 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. The blood sedimentation rate was 5.0 mm. in 1 hour. Blood Hinton and Wassermann tests were negative. A catheterized urine specimen contained 0.05 per cent of albumin. Blood smears revealed moderate sickling in stained and marked sickling in wet preparations after several hours.

DISCUSSION

Three of these 4 patients had had more or less severe joint pain in the past, but in none was there any residual damage in the joints. Vague muscle pain in the thighs and arms, unassociated with actual joint pain, had also been present. Since none of the patients were observed during an acute febrile episode with joint pain, it was impossible to check on the observation of others that salicylates, in contrast to their effectiveness in acute rheumatic fever, have only slight analgesic effects in sickle-cell anemia.

At the time of examination signs of cardiac embarrassment were not present except for slight dyspnea on exertion in Cases 3 and 4. One physical finding suggesting mitral-valve disease was present in all patients, namely, a loud systolic murmur, localized over the apex and transmitted to the axilla. In 3 patients, the murmur was louder than one would expect from the degree of anemia present; a thrill was not present. Slight enlargement of the left ventricle was present in 2 patients. A diastolic murmur was not heard in any patient but has been reported by Klinefelter³ and others. A systolic murmur over the aorta was present in Case 4. Slight prolongation of the PR interval was found in Case 4, and the general electrocardiographic picture was that of myocardial damage.

All the patients showed marked hypochromic anemia not responding to iron. The blood sedimentation rate was normal in 3 patients and slightly elevated in 1. Although this was not ascertained during acute attacks, a normal rate, if found during relapses, may prove of great aid in ruling out acute rheumatic fever. Such a rate is in conformity with experiments conducted by Bunting,⁶ who showed that sickle-shaped erythrocytes do not settle so fast as do normally shaped ones. In

sick ones, elevated blood sedimentation rates have been observed.

Although only the diagnosis of sickle-cell anemia alone could be established in our cases, the possibility of a combined occurrence of rheumatic fever and sickle-cell anemia should be kept in mind. In the absence of a mitral diastolic murmur, enlargement of the heart (mainly to the left) without characteristic configuration and a slow sedimentation rate, there is little likelihood of the presence of rheumatic fever. According to experienced observers, such a coincidence is extremely rare. Klinefelter³ mentions only one doubtful case. Walker and Murphy⁷ recently published a case verified by autopsy. Such a combination should be kept in mind, although for practical purposes it is improbable.

The well-known observation that heart failure frequently occurs in sickle-cell anemia remains to be explained. Most patients die either from heart failure or multiple thromboses. The tendency to thrombosis may lead to coronary occlusions, and the presence of myocardial scars in such cases may be due to myocardial damage following arterial thrombosis. Bauer⁴ stresses the frequency of right-sided failure due to thrombosis of the pulmonary vessels. Several such cases with terminal cor pulmonale are on record.⁸

SUMMARY

Four cases of sickle-cell anemia are discussed in which the diagnosis was obscured by the presence of polyarthritides and heart murmurs simulating rheumatic fever.

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It has long been known that a saccular aneurysm that is filled with clot — "Nature's cure" — may remain inactivated indefinitely. Blakemore and King have pointed out that blood circulating under pressure creates a strain on the wall of a saccular or fusiform aneurysm that varies with the square root of its surface area. A doubling of the diameter of an aneurysm by growth increases the total strain on the sac wall by 100 per cent. On the other hand, a blood clot, behaving according to the physical laws governing solids, reduces the strain on the sac wall of an aneurysm in strict accordance with the amount of fluid blood it displaces. The degree of clotting obtainable in an aneurysm depends, other things being equal, on the rate of blood flow through the aneurysm and the presence of an abundant clot-stimulating surface. Measurements of rate of flow in saccular aneurysms of equal size may vary as much as 300 per cent depending on the size of the mouth.

In the Blakemore and King's electrothermic method of coagulating aneurysms, fine, insulated coin-silver wire is introduced through a needle into the aneurysm in 10-meter segments. The protruding ends of a segment are connected with a direct current so regulated and calibrated against changes in electrical resistance of the wire on heating as to afford an accurate measurement of the temperature of the wire at all times and the rate of blood flow through the aneurysm on initial heating. Each segment of wire is finally heated to 80°C., which results in the deposit of a tenacious clot. On the basis of the number of amperes of current required to heat the first 10-meter segment to 80°C., it is possible to determine the variety of aneurysm (based on rate of flow) and approximately the number of segments that will be necessary to impede the blood flow to the point of occurrence of mass clotting. Blakemore and King have arteriographic evidence and proof from autopsy examinations that "brim-full" clotting can be obtained by this method in saccular aneurysms in which the diameter of the mouth does not exceed that of the sac. Experience so far has shown that this group behaves clinically as do cases of "Nature's cure." Experience with the method in treating syphilitic aneurysm of the thoracic aorta of the high-velocity, cup-shaped, saccular and fusiform varieties, although not showing a cure, indicates that clotting is frequently obtained to the degree of relieving strain on the sac sufficiently to permit the strengthening processes within the sac wall an opportunity to become effective. Particularly is this true in patients under forty-five years of age who are relatively free of arteriosclerosis. This is attested by the fact that several patients have remained symptom free for several years spent at hard labor in shipyards and munition factories. Aneurysms of the abdominal aorta of this type, including the arteriosclerotic fusiform aneurysm, may be inactivated by occluding the

aorta from within by wiring in two or more operative stages. The method affords a means of controlled clotting for gradual obliteration of the arteriosclerotic popliteal aneurysm without the complication of gangrene.

In the five-year period 1935 to 1940, Blakemore⁴⁶ used his method on 26 patients with syphilitic aortic aneurysm. Nine of these patients are alive, an average interval of seven years having elapsed since the operative procedure. The thoracic aorta was affected in 7 cases and the abdominal aorta in 2. Survival periods of the remaining patients ranged from a matter of hours up to eight years. The patient who survived for the full eight years had a fusiform aneurysm of the ascending aorta; he worked in a munition plant until four weeks preceding death, which was due to bronchial erosion and infection, with secondary hemorrhage. Following the wiring procedure nearly all the patients were relieved of their pain. In the absence of infection there has been only one rupture of the sac following the wiring in Blakemore's total series of more than fifty aortic aneurysms.⁴⁶ This is in sharp contrast to the high incidence of rupture — approximately 30 per cent — that accompanied the employment of the previous methods. Since poor risks were not excluded and since the patients had an associated syphilitic infection that in itself might have been fatal, the results appear to be encouraging. It is obvious that procedures such as blocking the sympathetic nerves should be used in association with the wiring procedure when indicated.

It should again be emphasized that the Blakemore operation is not the procedure of choice in all cases; for example, most peripheral syphilitic aneurysms should be treated by the Matas method. In summary, wiring and electrothermic coagulation may be used to inactivate syphilitic saccular aneurysms of the aorta, to slow the growth of high-velocity, cup-shaped and fusiform aneurysms of the thoracic aorta and to cause total occlusion of aneurysms of the abdominal aorta as well as to treat some of the peripheral ones.

BLOOD-VESSEL ANASTOMOSES

In the present war better means for preventing and controlling infection have made it safer to defer the amputation following injuries to extremities until the nutritional status of the part can be determined. Unfortunately, a number of the reports thus far show that the incidence of gangrene is higher than it was in the last war. This is probably due in the main to the more severe injuries that result from the destructive agents that are being employed. Although sympathetic block is of some value in increasing the circulation to an extremity in which the main vessels have been severed, there is frequently serious damage to the collateral vessels as well, and the benefit that results from blocking the sympathetic nerves and from the use of papav-

from 20 patients with *myasthenia gravis*. Only 2 of these patients had a thymoma. The results may be divided into five groups.

Four patients have died since the operation. In 3 cases death occurred within four days. In 2 of these, the patients were extremely ill at the time of operation and the procedure was carried out as a last resort. One patient died eight months after the operative procedure, having shown no improvement as a result of it.

Three of the remaining 16 patients are well or essentially well. Two of these have shown sustained improvement for more than two and a half years. One of the 3 patients had a thymoma.

Five patients are considerably improved. The dose of prostigmine has been very much reduced and the patients' general condition is much better than it was previously.

Five patients have shown slight improvement.

Three patients have exhibited little or no improvement.

The experience of Keynes and Carson³⁹ has been similar to ours. At the time of their report in 1943, thymectomy had been performed on 12 patients, and it is said that the series has now been extended to 25 cases.

Since some patients with *myasthenia gravis* have spontaneous remissions and since the results following thymectomy are not uniform, it is difficult to judge of the effects of this operative procedure on the course of the disease. The impression is gained that the removal of the thymus gland has been the cause for the improvement in a number of cases. Unfortunately, there are at present no means available for determining preoperatively which patients will be benefited by the procedure. Until further information is available, it appears that thymectomy should be performed only on patients with a severe degree of *myasthenia gravis* in whom the response to prostigmine medication is unsatisfactory.

PATENT DUCTUS ARTERIOSUS

Although it has been only a few years since Gross^{40,41} first successfully occluded a patent ductus arteriosus, the procedure has been accepted without reservations and is a noteworthy accomplishment. That this lesion is not a rare one is demonstrated by the fact that Gross³⁰ alone has operated on 65 persons with this abnormality. In fact, Keys and Shapiro⁴² estimate that there are approximately 20,000 people in the United States with an open ductus.

Since it has been demonstrated that this operative procedure can be performed with a low mortality rate, the indications for operation have been somewhat extended. The most conservative probably agree with Gross³⁰ that there are at least three definite indications for operation: when the patient

is not developing properly in physical stature; when there is any evidence of cardiac fatigue; and when there is superimposed *Streptococcus viridans* infection without evidence of peripheral emboli. Credit is due Touroff⁴³ for his work in establishing the value of operation in patients with endarteritis. In addition to the above-mentioned three groups, there remains a group of patients who are getting along well except for the constant danger of a future infection with *Str. viridans*. It is estimated by Gross³⁰ that such patients face a risk possibly high as 25 per cent of having a serious infection in the future. In addition to the danger of endarteritis, the open ductus in such patients may be causing symptoms that are not noted. The studies of Keys and Shapiro⁴² show that patency of the ductus arteriosus after the age of seventeen is associated with an average reduction in life expectancy about twenty-five years. Gross³⁰ has this to say about the results of operation on those patients who have been relatively free of symptoms:

I have been increasingly impressed by the statements of some of these patients after operation. Many of them have volunteered the information that . . . whereas they had no complaints before operation, . . . they now feel much better than they did previously; they have an increased vigor, their breathing is easier, their energy is greater and so forth. In other words, their circulation has been improved and they have become conscious of the change.

The frequency with which this operative procedure will be performed in the future will be influenced to a considerable extent by the success or failure of penicillin or some similar agent in the treatment of infection due to *Str. viridans*. Even if such infection does respond to penicillin, there will still be many patients with a patent ductus in whom operation is indicated.

From the viewpoint of operative technique, the main question at present is whether one should simply ligate the ductus or whether it should be completely divided and closed. Gross⁴⁴ now favors the latter course. Division and closure of the ductus is a better surgical procedure, but at the same time is a difficult and rather dangerous operation.

WIRING AND ELECTROTHERMIC COAGULATION OF ANEURYSMS

It has been approximately eighty years since the first attempt was made to wire an aneurysm, and has been fifty-six years since Matas first performed his procedure known as "endo-aneurysmorrhaphy." As regards improvements in methods for wiring aneurysms, the advances that have been made by Blakemore and King⁴⁵ have not been fully appreciated. Their procedure is so different from that used previously that it cannot be considered in the same class, and this contribution rates as one of the greatest in surgery in the last decade. All aortic aneurysms should be treated by this method as should peripheral aneurysms on an arteriosclerotic basis in the older age group.

completely interrupted; otherwise the secretion of sympathin at their endings is capable of exciting contraction in all the denervated smooth-muscle cells in the vascular walls. Smithwick⁵⁴ has described an excellent method for preganglionic sympathectomy of the arm and for the prevention of regeneration. He advises division of the chain below the third thoracic ganglion and intradural division of the second and third thoracic anterior spinal roots so that their subsequent growth will be checked by the intact dura. The mobilized upper portion of the trunk is covered with a cylinder of fine silk and the free end is transplanted into the muscles of the back in order to prevent reconnection of the divided ends. Despite all precautions, recurrence of vasoconstrictor tone occasionally takes place, but it can be stated that the results are much better now than previously.

Other types of vascular disease. In occlusive vascular disease of the extremities there may be superimposed vasospasm that is the deciding factor in leading to gangrene. It is important to realize that sympathectomy may bring about decided improvement even though preliminary tests do not indicate that such would be the case. Trimble,⁵⁵ Shumacker⁵⁶ and others have reported the cases of a number of patients with uncomplicated arteriosclerosis who have been benefited by sympathectomy. There is frequently a large element of vasospasm in thromboangiitis obliterans, and sympathectomy is often helpful. This procedure may be combined with the crushing of peripheral nerves. The use of sympathetic block in the treatment of thrombophlebitis was considered by Ochsner⁵⁷ in a previous Shattuck Lecture. Ligation of the major arteries of extremities had best be accompanied by measures that result in a local abolition of vasoconstrictor tone. In this manner the incidence of gangrene can be greatly lessened.

Sympathectomy in Essential Hypertension

Even though sympathectomy has distinct limitations in the treatment of hypertension, there is no doubt that there are many patients who have been definitely benefited. Only an occasional patient over fifty years of age is a suitable candidate for this procedure. Sympathectomy should not be performed when both cardiac and renal functions are significantly impaired. Grimson⁵⁸ has pointed out that the lowering of the blood pressure is usually directly proportional to the extent of the sympathectomy and inversely proportional to the severity of the disease. Four general types of operative procedures are in current use: supradiaphragmatic ganglionectomy and splanchnicectomy, as described by Peet⁵⁹; the subdiaphragmatic operation of Allen and Adson⁶⁰; the combined thoracolumbar sympathectomy of Smithwick⁶¹ and the total sympathectomy of Grimson.⁶² The first two procedures do not completely denervate the lower part of the body.

There has not been sufficient experience as yet to determine whether the more radical procedure of Grimson produces better results than does that of Smithwick. The latter procedure has yielded excellent results, and at present it appears to be the operation of choice. No doubt Smithwick's good results can be explained in part by a careful selection of patients.

Despite much work in recent years on the etiology of hypertension, understanding of the condition in man remains extremely inadequate. There is not even certainty as to the manner in which sympathectomy exerts its beneficial effects. The likeliest explanation is that there is a general reduction of the tone of smooth muscle in the denervated vascular bed.

THE PANCREAS

In the past the main deterrent to operations on the pancreas was the unfounded but firm conviction on the part of surgeons that operative trauma to the pancreas was fraught with great danger of producing acute pancreatitis, which in itself entailed a high mortality. It is indeed difficult to understand how this conception gained such widespread adoption in view of the fact that throughout the past decades cases of incision of the pancreas with excision of tissue, but without the production of pancreatitis, were reported in the literature from time to time.

Recent years have witnessed the development of the surgery of pancreatic tumors. The surgery of pancreatic inflammations has received relatively less attention because of the rarity of these conditions. The advent of the blood amylase test for acute pancreatitis has resulted in an improvement in diagnosis. Experience indicates that acute primary hemorrhagic pancreatitis is probably best treated conservatively rather than by operation and drainage of the region, as was the custom in the past when such a diagnosis was made.

In regard to the surgery of pancreatic tumors, the important factors in its development were the description of the syndrome of hyperinsulinism due to islet-cell adenomas and the spectacular cures obtained by their excision; the ever-increasing boldness of surgeons in extending surgical attack on intra-abdominal cancer, and the realization that survival is possible in man without the duodenum and the head of the pancreas, with consequent occlusion of external pancreatic secretion. As regards the second of these factors, advances in the understanding of surgical shock, the use of vitamin K and an appreciation of the importance of the nutritive state of the surgical patient have contributed to the feasibility of procedures that formerly could hardly have been carried out.

The following are a few of the many important contributions to this subject: the description of hyperinsulinism by Harris⁶³ in 1924; the report by Wilder and his associates⁶⁴ in 1927 of the first case of insulin-producing islet-cell carcinoma, which was

erine is not sufficient to prevent gangrene. The importance of this problem of gangrene and amputation has been appreciated by Blakemore and his associates, and their studies on this subject are of great interest. Eighty per cent of all wounded men in World War I had injuries of the extremities, and the extensive use of land mines and fragmentation shells at present indicates that the incidence in this war will continue to be high.

Blakemore, Lord and Stefko^{47, 48} have devised a nonsuture method for anastomosing the ends of severed arteries that consists in using vitallium tubes as a prosthesis for vein grafts. Long defects in vessels may be bridged. The method is simple and the anastomosis can be performed quickly. A moderate disproportion between the diameter of the vein graft and that of the artery does not prevent a successful result. It has been shown that preserved veins that have been prepared by quick freezing in a mixture of alcohol and dry ice and kept in the frozen state function effectively as grafts. Furthermore, homotransplants of vein grafts as well as autotransplants serve to prevent the development of gangrene.

Blakemore, Lord and Stefko⁴⁷ have had remarkable success in the experimental use of their method in conjunction with débridement and chemotherapy in badly contaminated wounds. The severed femoral arteries of dogs were repaired by use of the vein graft twenty-four hours after the vessels had been ligated and divided without aseptic precautions. Despite the fact that contamination was present and that anticoagulants were not used, 85 per cent of the anastomoses remained patent. Clinical experience with the method has confirmed the experimental observations. The relative freedom of the method from complications is thought to be due to the nonirritating qualities of the vitallium and to the fact that, since no sutures are used, the flowing blood comes into contact only with intima. It is evident that many extremities that would otherwise be lost can be saved by the employment of this method.

Blakemore⁴⁹ emphasizes the importance of including the use of heparin in the program for handling the wounded extremity with damage to the main artery. After good hemostasis has been obtained, preferably without the use of a tourniquet, measures for the control of blood clotting should be instituted in order to preserve the patency of undestroyed collateral vessels. These measures include the injection of 10 mg. of heparin—together with 50,000 units of penicillin—into the distal end of the severed and ligated main artery and the subcutaneous injection of 150 mg. of heparin in Pitkin's menstruum (Loewe's method). The clotting time is thereby prolonged for forty-eight hours.

In connection with the problem of the saving of injured extremities, the studies of Allen,⁵⁰ Brooks and Duncan⁵¹ and others on the effects of tempera-

ture on the survival of anemic tissues are of great importance. It has been shown that cooling a part with impaired circulation is effective in delaying or preventing the onset of gangrene. There seems to be no doubt that harm may result from surrounding an extremity with defective circulation by containers filled with hot water.

Thus it seems that the treatment of severe injuries of extremities with destruction of part of the main artery should include careful hemostasis, treatment of shock, débridement, chemotherapy, relief of vasospasm by papaverine hydrochloride and sympathetic block, heparinization, cooling of the part and bridging of the defect in the artery, if such is present, by Blakemore's nonsuture method, which employs a vitallium tube lined by a vein. Irrespective of the extent to which one is able to attain the ideal in the treatment of war wounds, the opportunity is certainly available for improvements in the therapy of wounds that are seen in the civilian practice of surgery.

AUTONOMIC NERVOUS SYSTEM

An excellent review of progress in surgery of the autonomic nervous system was recently presented by White,⁵² and the reader is referred to it for details. As White has stated, in no other field is the surgeon more indebted to the contributions of the anatomist and the physiologist. Only the advances in the treatment of peripheral vascular disease and of hypertension will be considered, and the review by White will be quoted freely.

Sympathectomy in Peripheral Vascular Disease

Raynaud's disease. The generally accepted explanation for the typical advanced case of Raynaud's disease is that proposed by Lewis⁵³; namely, that the phenomena of intermittent color changes in the digits are due to abnormal contraction of the arterioles in direct response to cold. The most interesting therapeutic problem is connected with the fact that vasoconstriction is nearly always abolished in the lower extremities after resection of the lumbar ganglia, whereas such was frequently not the case in the upper extremities after resection of the upper dorsal ganglia. It has been shown in man that the highest vasoconstrictor fibers to the upper extremity emerge in the second thoracic nerve and are present in each succeeding anterior root down to the ninth or tenth thoracic level. The difference in the earlier results with upper dorsal and with lumbar sympathectomy seems to have been explained satisfactorily on the basis that postganglionic fibers were interrupted in the dorsal region and preganglionic fibers in the lumbar region. The second and third lumbar ganglia carry only preganglionic fibers to the sciatic nerve, and their removal produces a defect of sufficient length to prevent regeneration. The sympathetic vasoconstrictor fibers must be

ns. In the meantime, the neurosurgeon as well as the osteopath has invaded the field of the orthopedic surgeon, and this is probably a good thing for the patient concerned, including the patient.

In the future every effort will undoubtedly be made to explain the failure to relieve symptoms. It is noted following some of these operations another problem of interest is the role of the cervical intervertebral disk as a cause of brachial neuritis. The absence of compression of the spinal cord. Inter's⁷⁵ opinion on this subject is as follows:

I believe we shall hear more of it in the future and that the number of cases operated on will increase. The problem is still in its infancy, but the number of cases that have been operated on during the past ten years means that it is a real entity and one of considerable importance.

This statement is supported by a recent article by Curling and Scoville.⁷⁹ These problems will be of particular importance in the post-war era.

* * *

As indicated previously, the advances in surgery are so numerous that one can consider only a few of them in a limited time and space. I have chosen those problems that seem of particular interest to me at the moment, and it is likely that others would select an entirely different list. Included among other contributions that might have been considered are the following: the compression treatment of burns; the Orr-Trueta treatment of open wounds and compound fractures; the use of concentrated human serum albumin and of gelatin; the development of thrombin, fibrin foam, and fibrin films; the use of heparin and of dicumarol; the intraintestinal use of poorly absorbed sulfonamides, such as sulfaguanidine and succinylsulfathiazole; the introduction of thiouracil for the treatment of hyperthyroidism and the preoperative preparation of patients who do not respond to iodine; the development of mechanical dermatomes; improvements in transurethral prostatectomy; concentration radiotherapy in the treatment of cancer of the larynx; irradiation of adenoid tissue in the prevention and treatment of deafness; studies on the Rh factor; the recognition and treatment of intracranial aneurysms; the diagnosis and treatment of tumors of the adrenal cortex and medulla; the treatment of Addison's disease by the subcutaneous implantation of pellets of desoxycorticosterone acetate; the intracranial approach to orbital tumors; improvements in mechanical devices for treating fractures; the development of methods that are aimed at stimulating the collateral blood supply to the heart; studies on the pathogenesis and treatment of blast and crush injuries; improved methods for nerve anastomosis; additional methods by which skin grafts may be held in place, the use of vitamin K; the wide employment of tetanus toxoid; and the use of vitallium tubes in the anastomosis of ducts.

Even this long list could be extended almost indefinitely.

One of the most gratifying features of surgery is that the solution of one problem simply opens up additional problems. Churchill⁸⁰ in discussing renal failure in association with injuries stated recently, "It has always fascinated me in clinical surgery to see that as one or more weak links in a chain are strengthened by improved methods of therapy, another weak spot is revealed that becomes recognized only because the chain holds to test it." There are numerous unsolved major problems. For example, it is now technically possible to remove various organs and parts, but it is impossible to replace these structures by those from another person. The technic for transplantation is suitable in most cases, but the part does not survive long in the new host. The solution of this problem would open vast possibilities. It is inspiring to realize that, despite the rapid progress and the many accomplishments in various fields, surgery still offers to investigators and clinical surgeons rich opportunities for work and study.

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found to be inoperable because of metastases; the report in 1929 of the first correct preoperative diagnosis of insulin-producing islet-cell adenoma by Howland,⁶⁵ with successful extirpation by Graham; the paper by Whipple, Parsons and Mullins⁶⁶ in 1935 that reported successful treatment of carcinoma of the ampulla by partial duodenectomy and excision of a wedge-shaped portion of the head of the pancreas; the report by Brunschwig⁶⁷ of the successful total extirpation of the duodenum and the entire head of the pancreas for carcinoma of the pancreas; the recent report by Priestley, Comfort and Radcliffe⁶⁸ of successful total pancreatectomy for a small-islet tumor, which interestingly enough has been followed by a relatively mild degree of diabetes; and the work of Dragstedt and his associates⁶⁹ with lipocaic. An index to the increasing frequency with which the Whipple procedure or a modification of it is being performed is afforded by the fact that Cattell⁷⁰ has performed seventeen such operations in the last several years.

Problems in operative technic at present center around procedures to reimplant the transected neck of the pancreas into the bowel. It has not yet been finally demonstrated that the successful anatomic implantation affords a functional result. There is some evidence that cicatricial occlusion of the transected neck may prevent its accomplishment. The observation in dogs that pancreatic ducts rapidly regenerate to bowel certainly does not apply in monkeys and has not been demonstrated in man.

Some persons get along normally with completely occluded pancreatic ducts and without the duodenum, others seem to lack full digestive powers for fats and protein but manage to get along well anyway, and still others also lack these powers but do very poorly. Attempts at substitution therapy for pancreatic juice are only partly successful, and here again the situation in animals differs sufficiently from that in man so that the answer can be found only by further clinical investigation.

Cancer of the body and tail of the pancreas is possibly one of the most difficult abdominal cancers that the surgeon has to deal with because it is so often "silent" until an advanced stage. Considerable experience will be necessary to permit an evaluation of what can be accomplished by these operations.

CARCINOMA OF THE PROSTATE

Following the work of Gutman, Sproul and Gutman⁷¹ and others on the prostate-phosphatase relation, Huggins and Hodges⁷² treated a number of patients with advanced prostatic cancer by removal of the testes or by estrogen administration, using as a yardstick the elevated serum phosphatase levels. The reduction in androgens was accompanied by a sharp fall in the amount of acid phosphatase to or toward normal and by a slower rise of alkaline phosphatase, which subsequently likewise decreased.

It was the impression of Huggins that the changes in alkaline phosphatase reflected healing in the lesions in bone. Clinical changes in some of the patients included the relief of pain, an increase in appetite, a gain in weight and a decrease in the size of the neoplasm. In several patients there has been recovery from paralysis that was due to involvement of the spinal cord or nerve trunks with cancer. Huggins⁷³ recently summarized the results as follows:

It must be emphasized that the results are not uniformly successful and that they fall into three groups: one group, less than 5 per cent of patients, received no or slight benefit from endocrine treatment; the other groups, larger and nearly equal in number, obtained respectively an improvement pronounced but unsustained (less than eighteen months) or a pronounced and more prolonged regression of the disease.

In a recent personal communication Huggins stated that about 25 per cent of the patients seem to be completely free of the disease more than three and a half years after orchiectomy.

If one grants that untreated carcinoma of the prostate gland in many cases follows a peculiar course, the observations of Huggins are extremely important. His work casts doubt on the concept of autonomy of the cancer cells, since he has found that in some cases prostatic cancer is dependent on androgen for its survival. The fact that this one type of cancer is sometimes amenable to general methods of therapy encourages one to hope that the same may be true of other forms of cancer.

RUPTURE OF AN INTERVERTEBRAL DISK

There is no problem that has excited wider interest and more controversy in recent years than that of the role of the ruptured intervertebral disk in the causation of low-back pain and sciatica. Middleton and Teacher,⁷⁴ Dandy⁷⁵ and others had described ruptured disks, but it was not until 1934 that Mixter and Barr⁷⁶ reported observations that led to an appreciation of the frequency of the condition. There is considerable difference of opinion concerning the accuracy with which a diagnosis can be made. Most observers are agreed that the introduction of radio-opaque substances into the spinal canal is rarely justified. In the last several years there have been noteworthy improvements in the operative procedure; these include a transition from a complete laminectomy with transdural removal of the disk to a unilateral exposure between the laminae, with removal of little or no bone, depending on the size of the opening, and extradural removal of the disk.⁷⁷

There is no doubt that ruptured disks do occur, and the wide differences of opinion have to do with the frequency of occurrence and the certainty with which an accurate diagnosis can be made. Time and further experience will show that the truth lies between the very reserved position that is taken by most orthopedists and the much more enthusiastic concept that is held by some neurosur-

er low, and R_4 was small and upright. The ie gave a + test for albumin, and the sediment tained 2 white cells per high-power field. The te-cell count was 19,800, with 88 per cent neutro- s. The sedimentation rate was 22 mm. in sixty utes. Two van den Bergh tests were negative : basal metabolic rate was normal. Plain films he abdomen and dorsal spine and gall-bladder lies were normal. The pain was relieved by ng. ($\frac{1}{2}$ gr.) of codeine.

During the next eighteen days the patient im- ved considerably, with almost complete dis-

pulsations were visible in the ascending portion but not in the descending. The back pain subsided somewhat, although movement of the back aggra- vated the pain. The urine cleared up, the white- cell count became normal, and the pulse ranged about 70. The patient was discharged to a nursing home on the thirtieth hospital day.

Second admission (four years later). After dis- charge the patient retired from work but carried on active life until about two months before re- entry, when, following the death of his mother, he noted marked shortness of breath and weakness

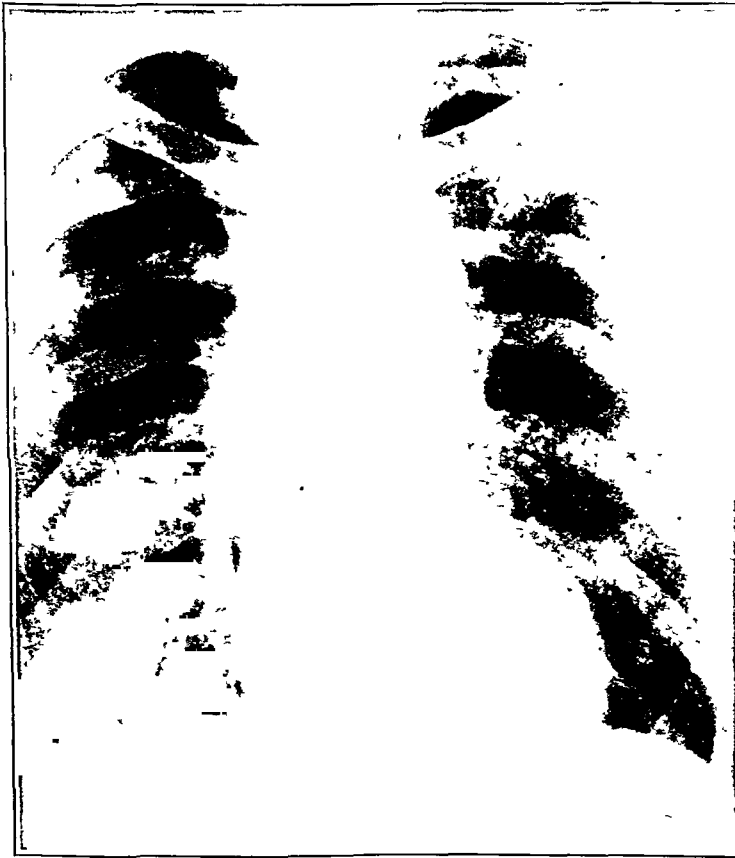


FIGURE 1.

pearance of the epigastric pain and fewer sweats. continued to have bilateral back pain. During t period a gastrointestinal series was entirely ative. Films of the chest, nine days after ad- sion, showed definite dilatation of the aorta, ich seemed to be more marked than in the pre- us examination, but whether this was due to the ht rotation of the patient or to actual dilatation ld not be determined. The dilatation was most rked in the upper descending portion, where the meter was almost twice normal. Fluoroscopic

on climbing stairs. He developed a sore throat. For the few weeks prior to admission he had raised considerable gas after eating. During that period he had two attacks of nocturnal dyspnea and found it necessary to use three pillows when sleeping. He had had nocturia (three or four times) but no pain, indigestion, loss of appetite, nausea, vomiting or swelling of the ankles.

Physical examination showed a well-developed, well-nourished man in no distress. The lungs were clear. The left border of cardiac dullness was 10 cm.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 30341

PRESENTATION OF CASE

First admission. A fifty-four-year-old man entered the hospital because of severe epigastric pain.

The patient was apparently perfectly well until a few hours before entry, when he developed a sudden, severe, stabbing pain between the shoulder blades. It was soon noticed in the epigastrium, below and to the right of the umbilicus, and seemed to go through and through. The pain was constant but there were acute exacerbations. Nothing seemed to relieve or aggravate the pain. There were no other symptoms referable to the gastrointestinal, genitourinary and cardiorespiratory systems.

The past history was essentially negative except for an inguinal herniorrhaphy six years before entry.

Physical examination showed a well-developed, well-nourished, restless, slightly cyanotic man complaining of severe abdominal pain. The throat was moderately red. The trachea was in the midline. The lungs were clear. The heart was normal in size. The sounds were bounding, with frequent extrasystoles. The aortic second sound was greater than the pulmonic. The abdomen was distended,

*On leave of absence

with spasm and mild tenderness in the epigastrium but without any palpable masses. There was tenderness to percussion over the lower thoracic spine. The arterial pulsations in the groins and in the feet were of equal intensity.

The blood pressure was 220 systolic, 90 diastolic, in both arms. The temperature was 98.6°F., the pulse 100, and the respirations 20.

Examination of the blood showed a white-cell count of 13,500, with 88 per cent neutrophils. The red-cell count was 5,050,000, with 175 gm of hemoglobin. The urine was acid, with a specific gravity of 1.022, and gave a +++ test for albumin, a ++ test for diacetic acid and a +++ test for acetone. Three to four white cells and red cells were seen per high-power field. Several blood Hinton tests were negative.

X-ray examination of the chest (Fig. 1) showed clear lung fields. The heart shadow was at the upper limits of normal, but the apex was blunted. The aorta showed a moderate degree of tortuosity, with slight dilatation. An intravenous pyelogram was normal.

On the second hospital day the pain was less severe, and located in the epigastrium. It was somewhat relieved by 10 mg. (1/6 gr.) of morphine, together with 0.65 gm. (10 gr.) of aspirin and 30 mg. (1/2 gr.) of codeine. Intravenous fluids were administered. The patient had considerable sweating. He pointed to an area below and to the right of the umbilicus as being occasionally tender. On the third hospital day he complained of epigastric pain and distress. The abdomen became distended, but without tenderness or spasm. The temperature rose to 101°F. The extremities seemed cold and clammy, with profuse perspiration over the rest of the body. The lips were slightly cyanotic. An electrocardiogram revealed frequent auricular premature beats, with a rate of 80 and slight left-axis deviation. T₁, T₂, and T₃ were upright, T₄ was

ys before admission swelling of the ankles appeared and he became progressively more dyspneic. e was seen in the Emergency Ward, where additional digitalis, Mercupurine and ammonium chloride were administered, without any improvement. Physical examination showed a restless, dyspneic man with evidence of recent weight loss. He exhibited Cheyne-Stokes respirations. The skin was cool and moist. There was dullness at the lung bases posteriorly, with decreased breath sounds and tactile fremitus. The heart was about the same size as previously; it was "fibrillating" at a rate of 82. The sounds were booming and distant, and no murmurs were heard. Mild tenderness was elicited to the right of the umbilicus. The liver was palpable two fingerbreadths below the costal margin. Marked edema of the ankles and legs was present.

The blood pressure was 170 to 140 systolic, and 95 to 105 diastolic. The radial pulse was 66, the temperature 98.6°F., and the respirations 25.

Examination of the blood showed a white-cell count of 10,000, with 82 per cent neutrophils. The red-cell count was 5,060,000, with 15.6 gm. of hemoglobin. The urine specific gravity was 1.024, with a ++ test for albumin; the sediment contained 2 or 3 red cells and an occasional white cell per high-power field. The stools were negative. The vital capacity was 52 per cent of normal.

The patient was given a six-meal bland diet without added salts. Fluids were limited to 2000 cc. One-tenth gram (1½ gr.) of digitalis twice daily, as well as ammonium chloride and Mercupurine, was administered. He perspired considerably and seemed to be improving. He was then started on 5 drops of saturated potassium iodide solution daily. In the course of the next ten days the edema almost completely disappeared and the perspiration diminished remarkably. On the twenty-first hospital day, while sitting up in bed, he suddenly clutched his chest and fell back, and died a few minutes later.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: Apparently this patient's pain at its onset was localized in one place. It came on suddenly, starting in the back between the shoulder blades, was quickly noted after that in the epigastrium, and was extremely severe. Naturally one thinks right away that the pain was probably of cardiovascular origin. The story could go with an extensive dissection of the aortic wall, which is suggested by the diffuseness of the spread of the pain and by the sudden onset without other symptoms. I have never encountered a case of myocardial infarction with pain of this distribution. Of course the acute abdominal emergencies must be considered, such as ruptured peptic ulcer, gallstones, mesenteric embolism and even renal colic. But there is no previous story of trouble in the digestive tract or in the urinary tract, and there

was no vomiting. These subdiaphragmatic lesions must be borne in mind, however.

There was slight tenderness in the epigastrium and also in the back. The arterial pulsations in the groins were of equal intensity, all coming through. If there were a dissecting aneurysm of the aorta, one would expect diminished pulsations or the disappearance of the pulsation on one side or the other, as not infrequently happens. Perforation of an aneurysm into the iliac arteries would, however, permit such pulsations to be found in the leg arteries.

This man had hypertension, but there is no note of the blood pressure in the legs. The statement that the arterial pulses were apparently well felt in the legs suggests that there was hypertension there too.

There were occasional red cells in the urinary sediment, but there is no suggestion of active bleeding, such as one might expect with a renal calculus or infarct. And there was no history of hematemesis to point to a peptic ulcer.

The x-ray examination gives some indication of a hypertensive heart, but it was not very large—possibly in an early stage, with 100 gm. or so of extra weight, which produced little change.

The prolonged pain is not particularly diagnostic. We have no note about morphine on the first day.

DR. BENJAMIN CASTLEMAN: He was given 15 mg. (¼ gr.) of morphine when he first entered the hospital.

DR. WHITE: The electrocardiogram was essentially normal. It is hardly likely that acute coronary occlusion had occurred, but the record is consistent with the other diagnoses mentioned.

There was considerable, but not extreme, leukocytosis.

By fluoroscopy, pulsations were visible in the ascending portion of the aorta but not in the descending portion. I am not sure about the importance of that difference. I think that normally one sees pulsation more readily in the ascending portion of the aorta than in the descending.

DR. GEORGE W. HOLMES: I have selected some of the films that looked rather significant. This film, taken in 1940, shows hypertensive changes, a tortuous aorta and a round left border of the heart, which usually means hypertrophy of the left ventricle. It also shows rather bright lung fields, with a low diaphragm. In the oblique view, one can distinctly see the outline of the aorta; there is a good deal of magnification in this position, and the estimate of size is not too accurate. I can safely say that the patient had some dilatation of the aorta, not saccular or anything that one might interpret as an aneurysm. An abdominal film taken at that time shows part of the liver quite well, and I think that he had an enlarged liver. I cannot see anything definite in the gastrointestinal tract, and I judge from the report that it was negative. In

to the left of the midline in the fifth space. The auricles were fibrillating. The abdomen was negative.

The blood pressure was 198 systolic, 120 diastolic. The temperature was 98°F., the pulse 65, and the respirations 25.

Examination of the blood showed a hemoglobin of 13.6 gm. The nonprotein nitrogen was 30 mg. per 100 cc. The urine had a specific gravity of 1.024, with a +++ test for albumin, and the sediment contained many coarsely and finely granular casts, 20 white cells and 4 red cells per

Barium passed after some delay through the pylorus, filling a rather large duodenal cap, in the center of which a 0.8-cm. ulcer crater was visible. An electrocardiogram showed auricular fibrillation, with an average rate of 70. T_1 was inverted, ST_1 , ST_2 , and ST_4 were sagging, T_1 and T_2 were upright, and T_4 was sagging. There was slight left axis deviation.

The patient was given 0.1 gm. ($1\frac{1}{2}$ gr) of digitalis daily, as well as 0.1 gm. ($1\frac{1}{2}$ gr.) of aminophyllin. He was placed on a three-stage gastric diet, with 15 drops of tincture of belladonna after



FIGURE 2.

high-power field. A Hinton test in dilutions and a Wassermann test were negative. X-ray examination of the chest (Fig. 2) showed the heart markedly enlarged and particularly prominent in the region of the left ventricle. The aorta was extremely tortuous and was moderately dilated, particularly in the descending portion. A gastrointestinal series showed marked tortuosity of the esophagus, apparently due to adhesions of the esophagus to the arch. In the stomach, along the lesser curvature and opposite the angulus, a crater-like niche was sometimes demonstrated on compression.

meals. He did well. A gastrointestinal series sixteen days later did not demonstrate the lesion along the lesser curvature or a definite ulcer crater in the duodenum. He was discharged on the twenty-second hospital day.

Final admission (forty-eight days later). Following discharge the patient was asymptomatic, but one month before entry he developed diffuse lower abdominal pain that was not relieved by eating. He experienced increasing exertional dyspnea, almost nightly episodes of paroxysmal dyspnea and daily pain in the upper anterior chest. Ten

DR. ALLEN: So he did; but they do not mention afterward. Did it have any bearing, Dr. Jones?

DR. JONES: It is entirely possible that the pain was vascular in origin.

DR. WHITE: Does one get such diffuse pain in cases of mesenteric embolism?

it was considered in the differential diagnosis, we did not believe that he had mesenteric thrombosis.

DR. WHITE: I suppose that he would have had more abdominal evidence.

DR. ALLEN: Yes, I believe he would.

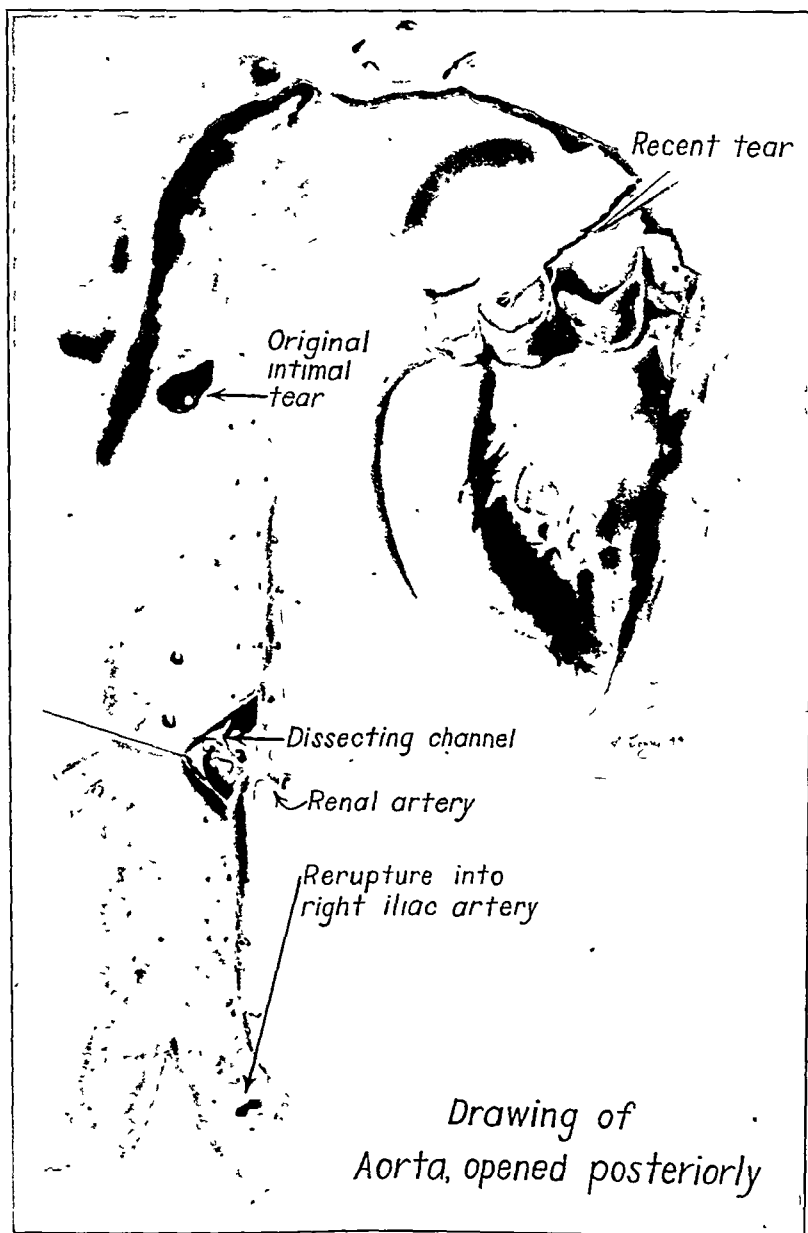


FIGURE 3

DR. ALLEN: The pain of mesenteric thrombosis is a little different in distribution as a rule. This pain was between the shoulder blades, which is a peculiar place to get pain caused by mesenteric thrombosis. If one is suspicious of that diagnosis, more is learned by the examination of the abdomen. Although

CLINICAL DIAGNOSES

Hypertensive heart disease.
Dilated aorta (?dissecting aneurysm of aorta).
Duodenal ulcer.
Thyrotoxicosis?

the 1944 films there is a marked change in the size of the heart but not in the shape. The aorta appears much as it did before: there is unusual tortuosity with some widening. I do not recall having seen many cases of hypertensive heart disease with such a large aorta. Also, it is wider in one place than in others.

DR. WHITE: The second admission was four years later. Nocturnal dyspnea appeared and increased, apparently the beginning of left ventricular failure in hypertensive heart disease. It is characteristic for these patients to have insomnia from pulmonary congestion, a point often overlooked. It might be well to point out that he still had a moderate degree of hypertension while in bed. I do not believe that we can use the blood pressure readily in differential diagnosis. A number of patients even with acute myocardial infarction have a higher blood pressure during pain than at any other time of their lives.

The red cells in the urinary sediment indicate either congestive heart failure or hypertensive renal involvement, or both.

The Hinton test was negative. They were looking hard for aortic dilatation with reference to syphilis. A gastrointestinal series showed marked tortuosity of the esophagus, apparently due to "adhesions of the esophagus to the arch." I am not familiar with that point. It is very interesting and one wonders whether it was due to aortic disease or to some mediastinal involvement.

DR. HOLMES: Tortuosity of the esophagus is not uncommon in elderly people. It does occur in some cases of chronic mediastinitis.

DR. WHITE: An inverted T₁ may be found in the electrocardiogram with either chronic hypertension or coronary heart disease. It does not necessarily mean coronary heart disease as we once thought it did. The sagging could have been the result of a digitalis effect. We do not know whether he had received digitalis before, but the patient was getting 0.1 gm. daily shortly after he had presumably been digitalized.

There was an interval of sixteen days between the two gastrointestinal series. Could the crater of a duodenal ulcer have completely healed in that short time? Perhaps one report or the other is in error.

DR. HOLMES: I think healing could have taken place in that length of time.

DR. WHITE: If he had had a duodenal ulcer could it have produced his symptoms? Not necessarily, nor his earlier ones either. I have no idea why he had abdominal pain unless perhaps it was from liver engorgement, spoken of later, which can sometimes give rise to pain in such a low position. The blood pressure was dropping, likely associated with a higher degree of heart failure.

The fluids were limited to 2000 cc. daily; 1500 cc. might have been better.

He was started on 5 drops of a saturated solution of potassium iodide. Why?

He did not die immediately, and death was not due to angina pectoris. There may have been an acute coronary occlusion, or ventricular tachycardia, or further dissection of the aortic wall, with rupture. I do not believe that a definite answer is possible concerning the exact nature of the final episode.

As for the final diagnosis, the patient certainly had hypertensive heart disease, with a big left ventricle and congestive heart failure. A healed dissecting aneurysm of the entire descending aorta with perforation into one of the iliac arteries, four years old, is quite probable, although it is almost too good a diagnosis to be true. A chronic double-barreled aorta is thought to be an extremely rare condition, but it was found in more than a quarter of Shennan's* 300 cases of dissecting aortic aneurysm, that is, a healed dissecting process with a double aorta. A duodenal ulcer, healed or healing, and terminal aortic rupture are also probable.

DR. J. H. MEANS: I can answer Dr. White's question about the potassium iodide. This man had staring eyes, lid lag and so on, and we wondered if, in addition to the rest of the picture, he had thyrotoxicosis. We thought it best to find out what his basal metabolic rate was. It was not diagnostic, but I thought it would do no harm to give potassium iodide on the possibility that he had thyrotoxicosis.

DR. CHESTER M. JONES: I should like to ask whether there is any evidence that potassium iodide is of value in the treatment of hypertension.

DR. WHITE: I believe not.

I should like to ask Dr. Allen to comment on the diagnosis of an acute abdominal emergency at the time of the first admission.

DR. ARTHUR W. ALLEN: I saw this patient in consultation at the time of the first admission, and I am afraid that I contributed little, aside from the fact that, to my mind, the case did not represent an acute abdominal emergency. I hazarded a possible diagnosis, which finally proved to be partially correct, and I also seriously considered the question of perforated ulcer. I do not recall all the physical findings, but I did not believe that the abdomen was boardlike enough to justify the diagnosis.

While I am speaking of this, I should like to ask whether the pain in the right lower quadrant could have had any bearing on the establishment of decompression of the aneurysm. If he had a fistula of the iliac artery, could that have been the cause of the pain in the right lower quadrant?

DR. WHITE: A dissecting aortic aneurysm, if that is the situation here, can explain almost any kind of pain because of the multiplicity of the vessels that can be involved. When this patient was first examined, however, he had a good femoral pulse.

*Shennan, T. *Dissecting Aneurysms*. Medical Research Council, Special Report Series, No. 193. London. His Majesty's Stationery Office, 1934.

the axillary line (Fig. 1). There was no hydro-orax. She improved in the next few days, but a repeat x-ray examination of the chest five days later showed little change in the appearance of the lungs. The density in the right lower lung field appeared to be confined to the right middle lobe. The trachea was extremely narrow, which had apparently been noted on one or more previous examinations. Flecky calcification was seen over the dome of the right diaphragm. The left costophrenic angle was obliterated. The improvement continued until seven days before entry, when she had a sudden attack of sharp pain in the right chest without fever or chills. She had a feeling of fullness

and pinpoint, and did not react to light or accommodation. The extraocular movements were normal. The tongue was dry, rough and red. The neck was stiff. The chest was barrel shaped. Over the right base posteriorly there was dullness, with bronchial breathing, diminished tactile and vocal fremitus and many rhonchi and rales. The left border of cardiac dullness was 8.5 cm. to the left in the fifth space. A Grade II apical systolic murmur was heard over the precordium but was not transmitted. The abdomen was mildly distended with gas. Some voluntary and involuntary generalized spasm was present. Peristalsis was diminished, and there was some tinkling of the peristaltic sounds. Consid-

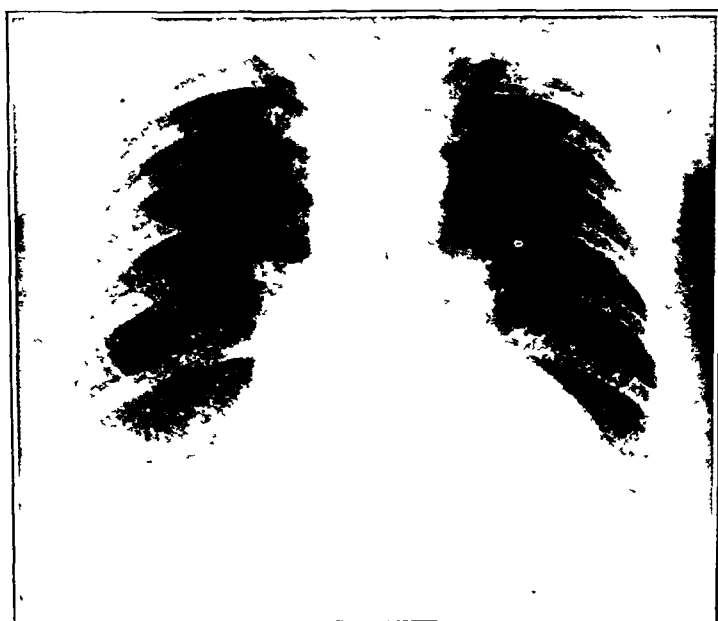


FIGURE 1.

in the pit of the stomach but no nausea or vomiting. The pain was relieved by the application of heat. She visited the clinic two days later, but refused hospitalization and returned home. She apparently stayed in bed, without eating or drinking much, gradually became disoriented and was found in a state of semicoma. She was then admitted to the hospital.

Four years before admission she had been treated for pernicious anemia. During that period she was discovered to have positive blood Hinton and Wassermann tests. About eighteen months before admission the spinal fluid was negative. She had had no history of primary or secondary manifestations of syphilis, and no treatment was given.

Physical examination showed a thin, poorly nourished, semicomatose woman. The skin was moist and warm. The pupils were round, regular

and mottling and cyanosis of the feet and fingers were noted. Neurologic examination revealed a right facial paralysis. The tendon reflexes of the left arm were more active than those of the opposite arm or of the legs; the plantar reflexes were normal.

The blood pressure was 180 systolic, 84 diastolic. The temperature was 99.2°F., the pulse 100, and the respirations 24.

Examination of the blood showed a red-cell count of 3,620,000, with 14.6 gm. of hemoglobin. The white-cell count was 23,800 with 98 per cent neutrophils. The urine specific gravity was 1.016, and the reaction pH 4.5; it gave a +++ test for diacetic acid.

The patient was placed in an oxygen tent and given 10 cc. of aminophyllin intravenously and 500 cc. of 5 per cent glucose in physiologic saline solution. She died nine hours after admission.

DR. WHITE'S DIAGNOSES

Hypertensive heart disease, with left ventricular enlargement.
 Congestive heart failure.
 Healed dissecting aneurysm of aorta.
 Peptic ulcer?
 Terminal rupture of aorta, with further dissection?

ANATOMICAL DIAGNOSES

Dissecting aneurysm of ascending aorta, recent.
 Dissecting aneurysm of descending thoracic aorta, healed, with rupture into right iliac artery.
 Cardiac hypertrophy, hypertensive type.
 Hydrothorax, bilateral.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed a hypertensive heart weighing over 800 gm. and there was about 600 cc. of clear, straw-colored fluid in each pleural cavity.

In the first portion of the descending thoracic aorta we found a large hole in the intima, which was smooth and shiny, certainly not ragged (Fig. 3). This communicated with a dissecting channel that went all the way down the aorta and re-entered the original stream at the origin of the right iliac artery, as Dr. White predicted. Here also the edges of the opening were smooth and shiny, indicating that the process was not recent. This old dissecting aneurysm had developed a new intimal lining, on top of which arteriosclerosis had been superimposed. Apparently the initial intimal tear, which occurred presumably in 1940, produced the bulging aneurysmal sac that was seen in the x-ray films. This aneurysm, which at first glance looked like the ordinary syphilitic aneurysm, was filled with a laminated thrombus, all of which was within the media and part of the dissecting process.

Just beyond the arch was another smaller but similar bulge, which also had an intimal opening. There was no communication between the two at the time of autopsy, and neither of them had ruptured externally. The dissecting aneurysmal sac had dissected around the mouths of the renal, intercostal and inferior mesenteric arteries and had lifted up the intima to produce some narrowing. There was, however, no dissection along these arteries.

The terminal event was an acute dissection of the aorta in the ascending portion, which is the commonest location. The intimal tear was transverse and was located just above the valve. It had dissected distally to include the arch and proximally as far as both coronary mouths. There was no external perforation, so that the sudden death may have

been anginal, owing to constriction of the coronary orifices.

DR. MEANS: I should like to ask Dr. White and Dr. Castleman if they think that the administration of iodide contributed to death by softening the aorta.

DR. CASTLEMAN: I doubt it.

DR. WHITE: So do I.

I should again like to call attention to the monograph written ten years ago by Dr. Shennan, of London. He reported 300 cases, 79 of which were old healed aneurysms. I looked them up last night because I was interested in how the patients died. I found a variety of ways, but most of them died of heart failure.

DR. ALLEN: Did any die because a surgeon tried to establish an iliac opening?

DR. CASTLEMAN: That has been tried in New York. The man lived a week.

DR. MEANS: What do you think the course of the blood was after this first aneurysm had taken place? Was the aneurysm acting as a channel as well as the aorta?

DR. CASTLEMAN: Without any question, but the aneurysm was small.

CASE 30342

PRESENTATION OF CASE

A sixty-four-year-old woman, a domestic, was brought into the hospital in semicomatose.

The patient was known to have had high blood pressure (230 systolic, 100 diastolic), an enlarged heart and a more or less chronic cough for several years. She had had dyspnea on exertion for the ten months before entry, during which period she had received 0.1 gm. (1½ gr.) of digitalis three times a day for one week, followed by 0.1 gm. daily. She was well except for occasional episodes of upper respiratory infection and cough. About seven months before entry, after one of these episodes of upper respiratory infection, cough and dyspnea, she was examined in the Out Patient Department, where x-ray films showed no unusual findings except for an enlarged heart. She was treated for cough and continued to receive 0.1 gm. of digitalis daily. Three weeks before entry, following another attack of upper respiratory infection in which she experienced considerable dyspnea, a feeling of extreme weakness, and cough productive of white phlegm, she was again seen in the clinic, where examination showed diminished breath sounds over the right lower lung field, with occasional expiratory squeaks. At that time the blood pressure was 220 systolic, 100 diastolic. The temperature was 99°F.; the pulse was 84 and regular. X-ray examination of the chest showed extensive increased density along the right border of the lung parallel to the diaphragm, and reaching from the lower aspect of the hilus almost to

he lobe was not smaller than normal, and even though no fever and cough are mentioned in the record, I think that they were overlooked. A white-cell count of 23,000 and 98 per cent neutrophils are definite signs of infection. I am no neurologist but looked up a few things and believe that the cranial-nerve signs on one side and the hemiplegia on the opposite side, the contracted, rigid pupils and the stiff neck are consistent with a lesion in the pontine area. Therefore I am going to say that this woman had a pneumonia of the right middle lobe, and that she developed suppuration in that lobe and that she died of a metastatic brain abscess in the pontine region.

DR. FREDERICH KLEMPERER: I followed this patient for the three years before entry. When I first saw her she was being treated for pernicious anemia and syphilis. It is questionable whether she ever had pernicious anemia, because when specific treatment was discontinued the red-cell count did not come down; in fact she had not received liver extract for three years. Antisyphilitic treatment was discontinued because of her generally poor condition — the marked hypertension and the fact that she was in and out of mild cardiac failure. The spinal fluid was negative. She had some neurologic signs — absent knee jerks and markedly diminished ankle jerks. She complained about paresthesias in the legs, but sensory examination was negative. The neurologic findings have never been explained.

I last saw her about ten days before she died, when she gave a story of cough and malaise, which had markedly improved by that time. X-ray examination was said to have shown atelectasis of the lower lobe, and I urged her to enter the hospital, but she refused. My impression was that she had either pneumonia or infarct and that the prognosis was poor.

DR. J. H. MEANS: Was a lumbar puncture done?

DR. KLEMPERER: Not at that time; the one done two years before was negative.

DR. MEANS: Did she have a positive Kernig sign as well as a stiff neck?

DR. KLEMPERER: Not so far as I know.

DR. MEANS: I suppose that the final episode was not related to the pulmonary situation. She may have had some kind of subarachnoid hemorrhage.

CLINICAL DIAGNOSES

Bronchiogenic carcinoma?
Bronchopneumonia?
Cerebral hemorrhage.

DR. PITTMAN'S DIAGNOSES.

Pneumonia, right middle lobe, with suppuration.
Metastatic brain abscess (pontine).

ANATOMICAL DIAGNOSES

Lobar pneumonia, right middle lobe (pneumococcus, Type 14).

Empyema (pneumococcus, Type 14).

Bacteremia (pneumococcus, Type 14).

Cerebral thrombosis, recent: left internal carotid artery.

Syphilitic aortitis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this patient showed an extensive empyema in the right chest, limited almost entirely to the region of the lower lobe. After the pus was aspirated we found that the middle lobe was completely solid. On section it showed the characteristic gray hepatization of lobar pneumonia. This process had extended partly into the right lower lobe; the lower portion of the lower lobe was not involved but was collapsed.

Microscopic examination showed a process that I do not believe could have been three weeks old; it probably began when she complained of pain in the chest about a week before she entered the hospital. What the process was at the time of the second x-ray film I cannot be sure. She may well have had an acute bronchitis with some atelectasis in the region in which the lobar pneumonia subsequently developed. We were able to recover a Type 14 pneumococcus from the pleural pus and the blood.

In the brain we found a fresh thrombus in the left internal carotid artery, with early softening of the cerebral hemisphere on that side. The bone marrow showed hyperplasia of the myeloid elements but no evidence of red-cell hyperplasia, so I think that we can rule out pernicious anemia.

She did have evidence of syphilis in that we found a mild aortitis with some narrowing of the coronary mouths.

DR. HOLMES: Was the trachea narrowed?

DR. CASTLEMAN: Yes, but we could not determine the cause; perhaps it was congenital.

DR. MEANS: Could you connect the cerebral and pulmonary affairs?

DR. CASTLEMAN: There was no infection in the brain.

DR. HOLMES: In the last film there is some evidence of fluid in the pleural space, but nothing like what you describe.

DR. CASTLEMAN: That film was taken the day before death. The empyema must have been present for at least three or four days, if not longer.

DIFFERENTIAL DIAGNOSIS

DR. HELEN PITTMAN: This woman had a great many things the matter with her, and the first point is to try to decide which are relevant to the terminal illness. She had apparently been treated for pernicious anemia four years before. I do not believe that that had much to do with the last episode. She was known to have positive blood tests for syphilis four years before, but a spinal-fluid tap eighteen months before entry was negative, and so long as she had no history of primary or secondary manifestations of syphilis and no treatment given, it is probably safe to assume that the pupils were not pinpoint and did not fail to react at that time. Discarding these things, we come to the final illness. She had been known to be hypertensive, with a large heart and more or less chronic cough, for a good many years. She had been ill for three weeks but had been well enough to come into the Out Patient Department and well enough to refuse hospitalization a week before she was brought in semicomatose to die in nine hours.

I am particularly anxious to see the x-ray films because apparently we can assume that the lung fields were negative until three months before the present illness, despite the fact that she had had a chronic cough for a good many years.

DR. GEORGE W. HOLMES: The diaphragm is high and the heart lies more or less horizontally in the chest, which tends to increase the size of its shadow regardless of the size of the heart. On the other hand, the curve of the left ventricle is prominent and enlargement is definite. In the lateral view the anteroposterior diameter of the chest is obviously increased, and the patient probably had some emphysema. Except for the low diaphragm and the absence of limitation of movements this is the type of chest that one sees in asthmatics.

In the area along the right border of the heart there is a definite change. From a right border well within normal limits in the first film, there is in the later film an indefinite hazy shadow that spreads out along the level of the diaphragm. In the lateral view this shadow lies in the anterior part of the chest and is thus in the region of the middle lobe. The other shadow, which extends along the axillary border, makes one suspect that fluid was present.

DR. PITTMAN: What do you think about the size of the lobe? Is it normal?

DR. HOLMES: There is little evidence of collapse. The diaphragm is not in the usual position. The heart, if anything, is away from the lesion rather than toward it, and there is no increased aeration in the portion of the lung above it, which ought to occur. I do not believe that there is any definite evidence of bronchial obstruction.

DR. PITTMAN: Do you see anything in the oblique view that you could possibly interpret as a cavity?

DR. HOLMES: The details do not show up well in this light, but there is no definite evidence of a

cavity. There are areas of calcification; I do not know what they are, and they are probably of no importance.

DR. PITTMAN: Do these shadows indicate dilated bronchi?

DR. HOLMES: I should not care to commit myself.

DR. PITTMAN: This is one of the times when the description of the films adds little to the description previously given. The question is, Which set of systems are we going to blame for this woman's final illness? She had a middle-lobe process. We have seen a great many middle-lobe pneumonias this year, but the patients either have recovered or still have something going on in the middle lobe without serious trouble.

This woman had a three-week illness, and we are told that she had an x-ray film taken seven months before entry that was essentially normal. The dry, rough, red tongue was, I assume, the tongue of dehydration, malnutrition and avitaminosis. I do not believe that it was the tongue of pernicious anemia. The blood pressure apparently dropped a good deal, which is not surprising. The patient entered the hospital semicomatose, with small pupils that did not react, a stiff neck and right facial paralysis, and these rather impressive signs point to something in the central nervous system. She had slight fever, and the pulse and respirations were only slightly elevated. She had a definitely elevated white-cell count—23,000, with 98 per cent neutrophils. The urinary findings I attribute to her nutritional state. The process in the chest was rather extensive, and yet I do not recall that any comment was made about cough or whether she was raising any sputum at the time of admission. With as much of a process in the chest I should have expected her to have cough and to be producing sputum. If sputum was not being raised because of bronchial plugging, I should have expected an elevation of temperature comparable to the leukocytosis of the blood.

So we come down to trying to decide whether this woman's terminal episode, which I am quite sure was cerebral, was on a vascular basis in a patient with known hypertension of many years' duration or due to infection. Whether she had a cerebral hemorrhage accompanying this pulmonary process or whether the terminal lesion was on some other basis, I do not know. I tried to see if I could get any leads from Dr. Holmes that would give a reasonably good cause for postulating a lung abscess. The chest was clear enough six months after entry to make us reasonably sure she did not have a long-standing bronchiectasis. We do know that one of the dangerous complications of lung abscess is cerebral metastasis and that this is one of the most frequent causes of death in such cases. Here, however, we have slim evidence on which to make a diagnosis of lung abscess. There was a definite process in the chest, which did not shrink the lung.

curring in building and equipping its hospitals; paid physicians' salaries ranging from \$4800 to \$14,000 and totaling \$500,000 per year; paid a similar total to staff nurses at the rate of \$150 to \$200 a month; provided the health-plan members with one of the most comprehensive coverages ever attempted; and treated a group of people definitely below par physically. No physical examinations were possible under union contract, but even if permitted, the shipyards would have been forced to employ practically all these workers because of the shortage of manpower.

The report goes on to mention the distrust with which the medical profession first looked on this financial plan. Gradually the profession became more tolerant as they recognized the tremendous load that the organization was carrying and the extraordinary conditions under which its job was being done.

The author of the report also goes on to discuss the future of the organization and the factors on which its continued existence must depend. The advantages to the workers and to the physicians of maintaining this or a similar medical service are enumerated. Details are also given concerning the quantity and quality of medical care furnished during the period covered by the report.

This report makes impressive reading and warrants more than a glance by physicians who are interested in the socioeconomic aspects of medical practice. Those who are now actively concerned with the problems of prepaid health and medical-care insurance may find it useful to adopt some of these methods and principles in order to obtain the most effective and efficient medical service to large numbers of people at low cost—and at the same time to maintain the high standards and dignity of the medical profession.

The conditions that make possible the establishment and maintenance of such an organization, however, appear to be comparable to those that occur in the Army and the Navy; that is, a large number of people in relatively good financial standing are herded into a new environment. What will happen when this wartime industry is disbanded or decentralized? How can this type of service be adapted to communities where reasonably adequate

medical and hospital facilities already exist, where many of the inhabitants seek hospitalization in terms of race and religion as well as medical competence and where they are working under the usual ups and downs that characterize small or moderate-sized industries? Can established practitioners and specialists adapt themselves to this type of medical care without serious disruption of such services? These are merely a few of the problems involved in adapting the Permanente setup to the one hundred and thirty million people of this country and to the doctors who must serve them.

SUTURE MATERIALS

OVER fifty years ago Halsted¹ described the fine silk suture technic in clean surgical operations and attested to its safety and efficacy. The method was accepted by few surgeons at that time, probably because it entailed such painstaking procedures and was so time consuming. Through the influence of Halsted's many pupils, however, as they scattered through the country and undertook important responsibilities, the technic gradually spread so that after forty years there were many nuclei, particularly in the teaching institutions, where this method of suturing was exactly carried out. At about that time the meticulous experimental work of Howes and Harvey² showed that catgut sutures, as they were then made and used, frequently disintegrated before the sutured tissues had gained any appreciable tensile strength through the processes of repair. In spite of this, catgut still continued to be used in the vast bulk of surgical practice.

Four years ago, Meade and Ochsner³ demonstrated that fine cotton sutures could be used in the same way that fine silk sutures had been used, and with equally good or better results. They also showed that the "lag period" in healing was reduced and that there was no period subsequent to suture when a wound in a healthy animal, correctly sutured with cotton, was any weaker than it was when the sutures were first placed. They also demonstrated that, even if a wound sutured in this way became infected, a permanent draining fistula associated with infection about the knots did not necessarily result, provided the cotton was not used for a continuous suture and provided that extremely fine

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PREPAID MEDICAL CARE A LA KAISER

THE Permanente Foundation Hospital has recently published its first annual report.* Starting with 6 physicians and 6 nurses on March 1, 1942, it opened offices in Oakland, California, and began to render industrial medical care to 20,000 men of two of the Kaiser shipyards. By the end of February, 1943, it was serving 90,000 workers and comprised a staff of 62 doctors, 241 nurses and 324 miscellaneous employees. It then had available 209 hospital beds, and construction of a 100-bed addition was begun later in the year. Three issues of the *Permanente Foundation Bulletin*, which contain

*Garfield, S. R. First annual report of the Permanente Foundation Hospital. *Permanente Found Bull* 2:35-48, 1944.

eighteen papers reporting clinical experience at the hospital by members of its staff, had already been published, and many other articles have appeared in various medical journals. These indicate a high standard of medical practice.

Some of the features of the report are worthy of study by all those interested in improving the standards of medical care and in providing it at a low cost to low-income and moderate-income groups. The history of the Permanente Foundation, its relations with the local medical profession, its financial statement and the medical services that it offers are reported in some detail. Some excerpts are as follows:

Our medical service and the Foundation were necessitated by the same motivating force that created the medical program for the armed services. That force was the displacement of masses of people to areas where existing medical and hospital services were inadequate.

We find that, where production for war created tremendous shifts in population, in the majority of instances medical and hospital care for these people was entirely forgotten. This was not so, however, where the armed forces directly entered production; for example, in Navy shipbuilding yards, Navy physicians, in uniform, were responsible for the care of the workers' health. When private industry was given the job, no such care was provided.

The Kaiser organization had . . . a knowledge acquired from past experience in providing medical and hospital care in industry. . . [It] had been engaged prior to the war in building huge construction projects in isolated areas such as Coulee Dam. With no pre-existing medical and hospital facilities available, these had to be provided to the many people employed. By trial and error, a method of highly satisfactory service was worked out through the years. After Pearl Harbor when the influx of war workers into the Richmond-Oakland area created a similar lack of hospital and medical facilities, it was evident that the tested solution which experience and time had proven efficient should be put into effect.

As a result Permanente Foundation was born. A charitable trust, with a Board of Trustees, headed by Mr. and Mrs. Henry J. Kaiser, registered in Alameda County, California, was set up in such a manner that there would be no profit incurred by anyone in the Kaiser organization. Any funds that may be accumulated by the Foundation must be used only for such charitable purposes as: medical research, provision of facilities in needy areas, medical care for the poor, rehabilitation of men returning from the war and so forth.

Economically, the results have been rather amazing. In spite of wartime difficulties, with the associated high cost of supplies and high salaries, while receiving only pre-war income from the employees, the Foundation has accomplished the following: retired \$500,000 of the debt of \$700,000

unction has been translated into the well-accepted principle that no person with positive sputum should be allowed to remain in a household where there are children. Too long, however, the danger of tuberculosis among school personnel has been overlooked although the school ranks immediately after the home in importance in the life of a child. The following statements, abstracted respectively from two recent publications (Laberge, L. *Detection of tuberculosis in schoolteachers in the Province of Quebec. Canad. Pub. Health J.* 34:125-129, 1943 and *Tuberculosis Control in the Schools of New Jersey*. Compiled by the New Jersey Tuberculosis League, co-operating with the State Department of Public Instruction, January, 1944) emphasize the problem.

* * *

The Legislative Assembly of the Province of Quebec on May 17, 1941, unanimously passed an act stating that no person can teach in a public, private or independent school unless he produces every year a physician's certificate stating that he "suffers from no infirmity or disease which renders him unfit for teaching" and "a certificate from a phthisiologist attesting that a clinical and radiological pulmonary examination shows that such person is free from tuberculous disease." Such examination must be made within two months following the engagement. Should any teacher prove to be tuberculous the contract to teach is immediately rescinded.

If Quebec glories in being the first province in Canada to pass such a law it must be admitted that it is the one to need it most — having the highest death rate from tuberculosis among the Canadian provinces. Three factors led to the passage of the law. First, a three-year educational campaign on tuberculosis that reached most of the population; second, a law passed by the City of Quebec requiring all teachers of the School Commission to undergo examination for tuberculosis, including films of the chest (out of 523 teachers examined 16 were withdrawn from teaching because of active or chronic tuberculosis). The third factor was a personal experience published in an educational review, which demonstrated mass contamination of pupils by a tuberculous teacher.

The legislation was introduced by the Council of Education, of which all the bishops of the province are members, so the doors of the teaching religious congregations were thrown open.

Difficulties arose in the enforcement of this new law as was to be expected, but these were overcome as the organization proceeded. In rural districts the expense was borne by the Board of Health, and in Montreal the Catholic and Protestant school commissions paid for the x-ray films.

The results of the examination of 16,524 teachers in the Province of Quebec, with the exception of the City of Montreal, are shown in Table 1.

It is apparent that tuberculosis was twice as prevalent among religious teachers as it was among the lay teachers, even though most of the religious congregations have re-

TABLE 1. Examination of Schoolteachers for Tuberculosis (Province of Quebec except City of Montreal).

TYPE OF TEACHER	No. EXAMINED	REJECTED FOR TUBERCULOSIS NO.	PERCENTAGE
Female:			
Religious	6,152	115	1.9
Lay	7,401	63	0.9
Male:			
Religious	2,155	27	1.3
Lay	816	7	0.9
Totals	16,524	212	
Average			1.3

quired, for the past few years, an x-ray examination of the chest from all applicants for admission to their groups.

In the City of Montreal, the results of examination for tuberculosis do not show the same trend. According to Dr. Laberge, the report was not complete for the religious teachers. The data from the Catholic School Commission are summarized in Table 2. The Protestant School Commission reported 1533 teachers x-rayed, only 1 of whom was rejected.

* * *

During August, 1939, an act passed by the Senate and General Assembly of New Jersey provided that the board of Education of every school district should periodically deter-

mine the presence or absence of active tuberculosis in any or all pupils in public schools. The rules and regulations for complying with this were to be made by the State Board of Education. Any pupil found with active tuberculosis was to be excluded from school until the disease was no longer communicable. Employees (which include teachers) of boards of education were required to have a physical examination by the provisions of a similar act passed at the same time. The State Board of Education was to determine the scope of such an examination.

The State Board of Education on May 11, 1940, ruled that all pupils of grades nine, ten, eleven and twelve and all special students enrolled in high school should be listed or

TABLE 2. Examination of Schoolteachers for Tuberculosis (City of Montreal — Catholic School Commission).

TYPE OF TEACHER	No. EXAMINED	REJECTED FOR TUBERCULOSIS NO.	PERCENTAGE
Female:			
Religious	1,879	3	0.16
Lay	906	6	0.66
Male:			
Religious	762	0	0.00
Lay	1,148	6	0.52
Totals	4,695	15	
Average			0.32

examined annually, as early as possible in each school year. For employees the board ruled that the examination was to be limited to determination of the presence or absence of tuberculosis.

This legislation was the climax of a long-term program of health education in homes, schools and community groups in New Jersey. Parents, children and school personnel were ready for the step when it was taken so there was no serious opposition in any county. The examinations themselves were used as an educational demonstration, and great care was taken to prepare pupils for them. It is now recommended that discussion with pupils should follow the testing. Answering students' questions and explaining the results in classrooms or individually will do much to give the procedure meaning.

X-ray examinations of the students who were positive reactors, and of a few students who were not tuberculin tested, revealed 343 cases of reinfection type tuberculosis or approximately 2 per 1000. Of the 2772 teachers examined, 67, or 2.4 per cent, had reinfection tuberculosis. Of these, 31 were classified as stable.

Reports on the disposition of reinfection type tuberculosis were incomplete. However, 23 patients were hospitalized, 21 were excluded from schools, 2 died shortly after examination and 40 students and employees were permitted to return to school under medical supervision with periodic x-ray examination.

Out of 195,130 students in New Jersey schools during 1941-1942, 19.9 per cent were positive reactors to the tuberculin test. Of 59,736 who were tested for the first time, 13.8 per cent were positive reactors. Retests of 99,964 students who were negative reactors in previous years yielded 10.7 per cent positive reactors. This group is highly significant from the standpoint of epidemiologic control. Its members have been recently in contact with an infection source. The prevailing infection rate in the school population therefore is slightly less than 20 per cent. Among teacher and employee group 39.7 per cent were positive reactors. Other significant chest, heart and orthopedic conditions were revealed by the school tuberculin testing and x-raying program. — Reprinted from *Tuberculosis Abstracts* (September, 1944).

BOOK REVIEW

A Catalogue of the Medieval and Renaissance Manuscripts in the Boston Medical Library. Compiled by James F. Ballard, director, Boston Medical Library. Sm. fol., 246 pp. Boston: privately printed, 1944.

The first impression in looking through the Boston Medical Library's new catalogue of incunabula and early manuscripts is that the volume has been planned — as every catalogue should be planned — to contain everything that

material with tiny knots accurately placed on small pieces of tissue was employed. These, of course, are the same criteria that Halsted set up for success with silk over fifty years ago.

Another defect of catgut was brought to light last year, when Dunham and Jenkins^{4, 5} showed that the tubing fluids with which most forms of catgut are impregnated contain highly irritating substances, which delay the process of repair.

A large dealer in surgical supplies has recently stated that the sales of silk and cotton for surgical use are rising by leaps and bounds and that the sale of catgut is stationary. Because of the fact that much of the silk and cotton for surgical use is bought through department stores, this statement assumes great significance. Of course, the manufacturers of catgut are improving their product, and catgut has a place in surgery, even in the work of those who are most enthusiastic in the use of nonabsorbable material. Such operations as those for hemorrhoids and for various types of gross infection will continue to need catgut, perhaps forever. Also, nonabsorbable sutures should never be buried in long strands, which means, for example, that the continuous suture used in the first layer for repair of the peritoneum should be made of catgut.

Any surgeon worthy of the profession should pride himself on his manual dexterity, and any busy surgeon with average dexterity, provided he is willing to devote a little care and thought, can quickly learn to use fine silk or fine cotton. The time may well be approaching when the use of catgut in routine operations will be the mark of a habit-bound surgeon.

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BLANCHETTE — William H. Blanchette, M.D., of Fall River, died August 1. He was in his seventy-second year.

Dr. Blanchette received his degree from Baltimore Medical College in 1896. He was a member of the American Medical Association.

HEAVEY — Thomas J. Heavey, M.D., of Med August 7. He was in his fifty-ninth year.

Dr. Heavey received his degree from the Middlesex School of Medicine, Waltham, in 1922. He was a member of the American Medical Association.

KICKHAM — Edward L. Kickham, M.D., of Boston died August 10. He was in his forty-ninth year.

Dr. Kickham received his degree from Tufts Medical School in 1923. He was a member of the medical and gynecologic staff of the Carney Hospital and St. Beth's Hospital, having been associated with the former in 1924 and with the latter since 1930. He had been in gynecology at Tufts College Medical School since 1924. He was a fellow of the American College of Surgeons, a member of the American Medical Association, the American Board of Obstetrics and Gynecology, and the Boston Obstetrical Society. He was treasurer of St. Luke's Church, Boston.

His widow, two brothers and a sister survive.

WAR ACTIVITIES

INDUSTRIAL HYGIENE

CHLORINE GAS HAZARDS IN ALUMINUM FOUNDRIES

The chlorine hazards in aluminum foundries have shown by a study made in California to be threefold:

Aluminum readily combines with the oxygen in air, releasing hydrogen gas, which collects in the interstices or porosities of aluminum in the melting pot. This is generally removed by passing chlorine through molten metal so that the hydrogen combines with chlorine to form hydrochloric acid. The excess chlorine discharged into the atmosphere above the melting unless removed by an exhaust hood, but the hood must be properly designed, or only a portion of the gas is removed.

The chlorine gas is introduced into the bottom of the melting pot by pipes connected to the tanks by lengths of rubber hose. These pipes may become clogged as the chlorine tanks are moved from pot to pot. As full tank pressure may exceed 100 pounds per square inch the rubber hose may leak or burst. Moreover, a chlorine tank may burst from overheating or from being tipped over, causing a fatality.

Gas burners under the melting pot are frequently vented, so that carbon monoxide concentrations may be as high as 50 to 75 parts per million and, as phosgene is readily formed from a combination of carbon monoxide and chlorine, there is danger of both carbon monoxide and phosgene poisoning.

Proper protection of the workmen requires a rather complicated system of control, consisting of venting of gas-burning devices, as well as much greater supervision of the method in which chlorine is handled. — Reprinted from *Industrial Hygiene News Letter* (July, 1944).

MISCELLANY

NOTE

The Hercules Powder Company has inaugurated educational tours to acquaint local physicians with working conditions to which their patients may be exposed. The first tour was made in Mansfield and attended by local physicians, representatives of the Massachusetts Division of Occupational Hygiene and the Committee on Industrial Health of the Massachusetts Medical Society.

TUBERCULOSIS IN SCHOOLS

The protection and education of children is universally conceded to be one of the primary functions of the modern state. In the realm of public health, especially that part which concerns itself with the control of tuberculosis, this

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CHRONIC LATENT HEPATITIS FOLLOWING CATARRHAL JAUNDICE*

MARK D. ALTSCHULE, M.D.,† AND D. ROURKE GILLIGAN, M.D.‡

BOSTON

THERE are now available in the literature records of the persistence of icterus,¹⁻⁸ as well as reports describing increased plasma bilirubin and decreased bilirubin excretory function⁵⁻⁹ in some patients who years previously had had an attack of catarrhal jaundice. Chronic gastrointestinal complaints⁵⁻⁹ and chronic hepatic enlargement⁵⁻⁸ have also been reported as sequelae of acute catarrhal jaundice. The present report of laboratory and clinical studies made in an unselected series of 36 persons who had had catarrhal jaundice one to twenty-nine years previously similarly demonstrates in some cases the persistence for years of certain evidences of hepatic dysfunction and affords information concerning the frequency of abnormal findings. This study was thought to be particularly pertinent at the present time because of the large number of cases of catarrhal jaundice in the armed forces of the present war; the incidence of the disorder in the War of 1812, the American Civil War, the Franco-Prussian War and World War I was similarly high. There is no complete accord in the interpretation of the clinical significance of so-called "chronic latent hepatitis" following catarrhal jaundice; the present study adds information bearing on this problem.

MATERIAL AND METHODS

The group studied was made up almost entirely of members of this hospital staff, students of the Harvard Medical School and of Harvard College and subjects who had been patients in this hospital at an earlier date when they had an attack of catarrhal jaundice. All these subjects had been observed during their episodes of icterus by competent physicians, including physicians on the staff of this hospital and in the Department of Hygiene of Harvard University. When actual hospital or physicians' records were not available, the symp-

toms and signs and the physician's diagnosis at the time of the attack were reviewed with the subject. The latter were, with one exception, scientists, technicians or medical students.

The bilirubin measurements were made by the method of Malloy and Evelyn, employing the

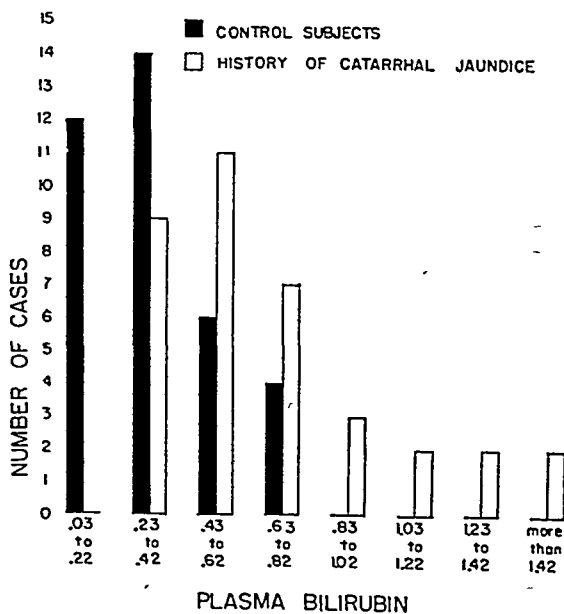


FIGURE 1. Plasma Bilirubin Levels in Persons with and without a History of Catarrhal Jaundice.

Evelyn photoelectric colorimeter.¹⁰ During the study the plasma bilirubin concentration was also measured in 36 normal persons with no history of hepatic disease and no signs of any visceral disorder. These subjects had plasma bilirubin levels ranging from 0.08 to 0.82 mg. per 100 cc., with an average of 0.31 mg., 32 subjects having values of 0.6 mg. or less (Fig. 1). These findings are essentially the same as those reported for normal subjects by Malloy and Evelyn,¹⁰ using the same method, and by Kornberg.⁸

*From the Medical Service and the Medical Research Laboratories, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

†Associate in medicine, Harvard Medical School; acting director, Medical Research Laboratory, Beth Israel Hospital.

‡Associate in medical research, Beth Israel Hospital; research associate, Harvard Medical School.

one needs and nothing more, in itself a bibliographical feat of high order. Its annotations, for instance, are a model of scholarly discrimination — brief, to the point, and present only when needed to emphasize information of importance. In addition to its seven hundred and twenty-six entries, there are three concordances and five indices. Thus it has been made not only a lean volume, but a well-rounded one.

The collection has as its purpose the gathering of such manuscripts and early printed books as might have been brought together in a fifteenth-century physician's library. Such, in fact, was the original aim of Dr. William Norton Bullard, whose collection, first through loan and then through bequest, forms the foundation upon which the library's collection rests. To his books have since been added purchases from the Bullard, the Godfrey M. Hyams and the John Warren funds, as well as from the library's general resources, with the result that the collection now totals fifty-two medieval and renaissance manuscripts, and six hundred and seventy-four early printed books.

As is to be expected, the majority of these are of medical interest. But, in rounding out the collection, the director has taken into consideration the fact that a physician of the fifteenth century no doubt had minor interests and hobbies, which would have brought books on other subjects to his shelves. For this reason, in Mr. Ballard's excellent subject-index, one finds occasional and intriguingly nonmedical books on architecture, geology, gambling, hunting, orations, inventions and canon law.

A library reproducing such a physician's interests, it seems, is not a hypothetical matter. As pointed out in Dr. Henry R. Viets's scholarly introduction to the catalogue, the manuscript collection follows closely the titles known to have been in the library of Giammatteo Ferrari da Gradi, who was professor of medicine at the University of Pavia from 1432 to 1472, as also the medical books in the scientific library brought together by Cardinal Nicolaus of Cues prior to 1464. Similarly, the fifteenth-century printed books run parallel to those known to have been in the collections of contemporary physicians, such as Hieronymus Münzer, Hartmann Schedel, Ulrich Ellenbog and Nicolaus Pol. In fact, the library actually has a number of books from Münzer's collection.

Through the medical incunabula upon the Library's shelves, it is possible to understand the status of medical science at the time of the invention of printing. "when the impounded waters of culture were let loose." Through the early manuscripts here assembled, it is possible to reconstruct the historical background upon which medical science then rested.

Collectanea Medica, a manuscript written by various physicians within the two-hundred-year period from 1250 to 1450, treats of a fascinating combination of subjects — eye and skin diseases, corns, "palsey," measles, gout, laryngitis, food and drink in relation to health and so forth. In addition, it includes a fourteenth-century prayer, written about 1350, to be pronounced by a physician when administering a remedy; and also a formula for extracting blue coloring from lapis lazuli which, interestingly enough, may have some bearing on the quality of the blue used in the beautifully illuminated borders and initial letters of the period. Another *Collectanea Medica*, written about 1450, contains treatises on the detection of disease, the plague, and the effects of the zodiac on blood-letting. A *Register Simplicium*, a manuscript of special interest, written in Austria in 1477, contains a long inventory of medieval drugs and materia medica.

On the opening page of the incunabula section of the catalogue there is an entry for the 1471 Jensen edition of Abulcasis. Bound with the library's copy of this work is Nicolaus Salernitanus's *Antidotarium* of the same press and year. Farther on in the text are noted later editions of Mesue's *Opera Medicinalia*, first printed in 1471, and of Pliny's *Historia Naturalis*, issued in 1469 and again in 1470. And prior to the Pliny came the *De Sermonum Proprietate* of Rabanus Maurus, undated but assigned to a Strassburg press before July 20, 1467. The last not only has its honored place upon the library's shelves, but it heads the list in Osler's *Incunabula Medica*, as the first "medical" book known to have been set in type. Thus, exclusive of single-leaf prints, the catalogue accounts for a half dozen of the first medical items

known to have been circulated in printed form. And among the early broadsides, the library is fortunate in possessing the rare third *Almanac* in German, a blood-letting calendar, assigned to the Zainer press at Augsburg about 1469-1470. Although part of its second column is lacking, the only other copy of the *Almanac* that is known (in Munich) has the second column intact, but lacks part of the first. Thus, the two copies together provide the complete text.

Among the books of anatomical interest are Peygh's *Compendium Philosophiae Naturalis*, the first printed anatomical treatise with illustrations; and Brunschwig's *Das Buch der Chirurgia*, printed at Strassburg by Grüninger in 1497. In the copy described, new matter has been added, including a brief tract on anatomy and a woodcut diagram of a skeleton. In view of the questions involved in the making up of this variable work, it is worthy of note that the library's copy — perfect, uncolored and in prime condition — is identified in Mr. Ballard's note as follows: "The first impression of the first edition [of *Das Buch der Chirurgia*] with the first printing of the added *Anatomia* as described by Sudhof Arch.f.d.Gesch.d.Med., Lpz., 1907-1908, 1:41. With 45 large woodcuts printed from 18 different combined blocks 13 small woodcut illustrations, and the full-page woodcut of the skeleton for the *Anatomia* adapted from the Helian broadside of 1493." Of even greater rarity is a broadside probably contemporary with the woodcut accompanying the *Anatomia* [early 1498?]. This represents a skeleton drawn with much artistic feeling, and engraved on copper by Zoot Andrea — a broadside of which only two other copies are known, and those both in Paris.

Six books were not registered as in the country in 1940, when the second census of incunabula in North American libraries was published. The Catalogue thus adds to our records the German *Almanac* already mentioned, a German edition of the *Ruralia Commoda* of Petrus de Crescentiis, the *Recollectae super Physica Aristotelis* of Galetanus de Thienis, the *Lunarium* of Bernardus de Granollachs, a *Tractat contra Pestem*, attributed to Heinrich Louffenberg, and the *Prothonotariomastix* of Paulus de Middelburgo.

By the cleverly economical phrases, "not in Osler" and "not in Klebs," used advisedly with a few entries, Mr. Ballard has given passing emphasis to a score or so of titles whose interest to medical science has made them in his opinion worthy of inclusion. Among them he notes the important *Bull on Burials*, issued by Bonifacius VIII, which, in its condemnation of the dismemberment of bodies of the dead, was for a time, until its re-interpretation, accepted as opposed to dissection and hence to the acquiring of direct anatomical knowledge.

In providing a subject-index for the volume, Mr. Ballard has made a very vital and important contribution to the study of incunabula. For early printed books, like other books, were originally published because of the timeliness of their subject interest. Various bibliographers, Dr. Osler foremost among them, have within fairly recent years segregated medical incunabula. Dr. Klebs has contributed still more to the classifying of incunabula by enlarging his survey of medical incunabula to include other sciences. But Mr. Ballard in his subject-index has broken down the broad classification into the specialized interests of the individual books. In other words, he has analyzed his incunabula just as modern books are indexed, thus making a contribution both to the study of incunabula and to the history of medicine. Here, in the catalogue of a collection brought together for the purpose of reproducing a fifteenth-century physician's library, is a subject-index of some two hundred entries. Thus the catalogue gives knowledge not only of physicians' books but of their contents as well.

It is a pleasure to find that publication of the catalogue has come at a time when Mr. James F. Ballard, director of the Boston Medical Library, has completed fifty years of service. The volume thus stands most fittingly as the culmination of his long years of scholarly labor.

It has been issued in an edition of four hundred copies, planned in an appropriate, clearcut format by Dr. Viets, the librarian, and printed by the George Banta Publishing Company of Menasha, Wisconsin.

(Notices on page xv)

ndice recover completely. The occurrence of ite or subacute yellow atrophy followed by uth or the development of clinical manifestations chronic cirrhosis of the liver has been observed occasional cases immediately after or shortly er an attack of infectious hepatitis; these imediate sequelae will not be discussed. That jaunde may be persistent in some patients following arrhal jaundice has also been stated previously a number of authors.¹⁻⁸ Studies of the plasma bilirubin concentration confirming this statement ive been recorded.⁵⁻⁸ In addition, impairment of ilirubin excretion after administration of bilirubin as been described by Soffer and Paulson,⁹ Kalk,^{5, 6} ad Kornberg.⁸ The results of the present study onfirm these earlier findings. Our observation at abnormally high plasma bilirubin values persted for years in 25 per cent of this series indicates higher incidence of chronic mild impairment of hepatic function following catarrhal jaundice than as been generally believed to exist. The fact hat impairment of bilirubin excretion is not inrequently demonstrated by the bilirubin-excretion est following catarrhal jaundice, even when there is no chronic hyperbilirubinemia,^{8, 9} indicates that the incidence of chronic mild impairment of liver function is even higher than demonstrated by the 25 per cent incidence of chronic hyperbilirubinemia in our subjects. This concept is supported by the observation that the distribution of the plasma bilirubin values of the 27 patients who had had catarrhal jaundice but had bilirubin values within the normal range includes an abnormally large number of values in the high normal range (Fig. 1).

The significance of the persistently abnormal hepatic function after infectious hepatitis is not clear. A wide variety of vague chronic complaints, including dyspepsia, abdominal fullness, upper abdominal discomfort, anorexia, heartburn, fatigue and belching, are described in such patients by Kalk,^{5, 6} Polack,⁷ Kornberg⁸ and, less emphatically, by Soffer and Paulson.⁹ Kalk⁶ also records complaints of a bad taste in the mouth, a feeling of tension, loss of ambition, headache, strong thirst, a craving for sweets and an aversion to alcohol and fat. In our own cases the icterus, when persistent, was not associated with chronic gastrointestinal complaints or a greater than normal incidence of acute gastrointestinal upsets; evidence of impaired utilization of vitamin A was, however, present in 2 cases. Enlargement of the liver, as well as that of the spleen in 1 case, was not associated with symptoms in these cases, although other authors⁵⁻⁸ described hepatic enlargement in many of their patients with a variety of gastrointestinal complaints following catarrhal jaundice. It should be emphasized that our subjects were unselected. Thirty-four of them came to our attention as a result of our own efforts to secure subjects recovered from catarrhal jaundice and not because they sought medical advj 2 cases, the subjects required

medical attention for symptoms unrelated to hepatic dysfunction.

The hepatic-histopathologic changes responsible for the evidences of retention of bilirubin in these patients are unknown. The prognosis also is not clear. The occasional occurrence of cirrhosis of the liver years after the apparent complete recovery from what appears to have been catarrhal jaundice has been noted by some clinicians,¹³ but, this must be an extremely infrequent occurrence if one is to judge from the relative frequencies of catarrhal jaundice and of hepatic cirrhosis.

It is concluded, therefore, that the chronic latent hepatitis that often follows apparent recovery from catarrhal jaundice is usually benign and unassociated with symptoms and is therefore not clinically significant; in rare cases it is the fore-runner of the clinical syndrome cirrhosis of the liver.

SUMMARY AND CONCLUSIONS

Studies of 36 persons who had had attacks of catarrhal jaundice one to twenty-nine years previously revealed hyperbilirubinemia in 25 per cent. It is probable that the incidence of impairment of liver function was even higher, since the distribution of plasma bilirubin values revealed an abnormally large number in the high normal range. Nine subjects in the entire group had palpable livers and 1 a palpable spleen. The chronic latent liver disorder revealed by this study was not accompanied by symptoms and did not appear to be progressive. It is concluded that a mild, benign form of chronic hepatitis is frequent after catarrhal jaundice.

We are indebted to Drs. Arlie V. Bock and Andrew W. Contratto, of the Hygiene Department, Harvard University, and Drs. Lewis Dexter and Lewis W. Kane, of the Harvard Medical School, for their help in obtaining many of the subjects of this study.

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OBSERVATIONS

Plasma bilirubin levels. The plasma bilirubin concentrations ranged between 0.23 and 3.01 mg. per 100 cc. in the 36 patients who had recovered from infectious hepatitis; 16 had values above 0.60 mg. and 9, values above 0.82 mg. — that is, higher than any value found in the group of 36 normal subjects (Fig. 1). Four patients had had two or three attacks of jaundice. There was no relation between the concentration of plasma bilirubin and

Symptoms. Except for one patient with active peptic ulcer, another with active colitis and a third with a history of irritable colon many years previous to this study, none of the patients, icteric or not, had any chronic gastrointestinal complaints or any unusual number of gastrointestinal upsets. None showed lack of stamina; many of the subjects were or had been college athletes, including the one with the highest plasma bilirubin found, — namely, 3.01 mg. per 100 cc., — who was at the time of

TABLE 1. Summary of Data.

CASE NO.	PRESENT AGE	DATE	FIRST ATTACK ICTERIC INDEX	PALPABLE LIVER	NO. OF ATTACKS	PERIOD AFTER FIRST ATTACK	PRESENT OBSERVATIONS			SYMPTOMS
							PLASMA BILIRUBIN LEVEL	ICTERUS OF SCLERAS	PALPABLE LIVER	
	yr.					yr.	mg /100 cc.			
1	21	1939	?	+	3	3	3.01	++	1 cm.	None
2	33	1920	?	?	1	21	1.97	+	1 cm.	Vitamin A deficiency
3	27	1936	90	1 cm.*	1	4 8/12	1.32	+	1 cm †	None
4	25	1926	?	?	1	15	1.24	+	0	None
5	18	1939	?	?	1	3 8/12	1.09	+	2 cm	None
6	24	1932	?	?	1	10	1.09	++	0	None§
7	20	1933	43	0	1	8	0.94	+	0	None
8	33	1928	?	?	1	15	0.89	0	0	Vitamin A deficiency
9	28	1932	?	0	1	9	0.85	0	0	None
10	35	1922	?	?	1	21	0.81	0	0	None
11	20	1941	?	?	1	2 6/12	0.81	0	0	None
12	29	1933	?	0	1	8	0.79	0	0	None
13	23	1938	100	?	1	2 7/12	0.79	0	0	None
14	22	1938	?	?	1	4	0.70	0	0	None
15	17	1937	50	0	1	3 7/12	0.63	0	2 cm.	None
16	33	1940	45	0	1	1	0.63	0	0	None
17	37	1917	?	?	2	25	0.61	0	0	Colitis for 3 yr.
18	20	1935	?	?	1	9	0.61	0	0	None
19	33	1913	?	?	3	29	0.54	0	0	None
20	35	1930	?	?	1	11	0.54	0	0	None
21	27	1922	?	?	1	20	0.54	0	0	None
22	27	1938	77	+	1	5	0.54	0	0	None
23	29	1940	60	3 cm.	1	1 1/12	0.47	0	2 cm	None
24	25	1936	?	+	1	6	0.45	0	0	None
25	21	1939	?	?	1	2 10/12	0.43	0	2 cm.	None
26	25	1922	?	?	1	20	0.43	0	0	Irritable colon for several years after attack
27	32	1938	?	?	1	5	0.43	0	0	None
28	42	1940	?	0	1	1 9/12	0.38	0	0	None
29	47	1922	?	?	1	20	0.38	0	0	Peptic ulcer
30	22	1936	?	?	1	6	0.33	0	0	None
31	48	1930	100	+	1	12	0.33	0	0	None
32	22	1940	35	0	1	1 1/12	0.31	0	1 cm.	None
33	63	1934	?	?	1	8	0.29	0	1 cm	None
34	22	1929	?	?	2	13	0.28	0	0	None
35	46	1928	?	?	1	15	0.25	0	0	None
36	57	1934	45	+	1	8	0.23	0	0	None

*Distance below costal margin

†Skin also icteric.

‡Spleen also palpable

§According to the patient's history, he had often had plasma bilirubin levels as high as 4.0 mg per 100 cc

the occurrence of multiple attacks, nor was there any correlation of the former with the elapsed time between the attack and the present study (Table 1). The scleras appeared slightly icteric in 7 patients, all of whom had plasma bilirubin levels above 0.9 mg. per 100 cc. A yellowish tinge to the skin was present in 2 patients.

Hepatic and splenic enlargement. The liver was palpable 1 or 2 cm. below the costal margin in 9 patients, only 5 of whom had plasma bilirubin levels above the normal range. The spleen was felt in only 1 case, in which the plasma bilirubin concentration was 1.32 mg. per 100 cc.

study a member of the Harvard crew. Two of the group, whose plasma bilirubin values were 0.89 and 1.98 mg., respectively, fifteen and twenty-one years after an attack of infectious hepatitis, had the skin changes of moderately severe vitamin A deficiency in spite of the ingestion of adequate diets.

DISCUSSION

The disorder known as catarrhal jaundice has been shown to be a form of hepatitis^{11, 12} apparently consequent to infection, although the causative agent has not been identified. It has been generally believed that almost all patients with

jaundice recover completely. The occurrence of acute or subacute yellow atrophy followed by either the development of clinical manifestations of chronic cirrhosis of the liver has been observed in occasional cases immediately after or shortly after an attack of infectious hepatitis; these immediate sequelae will not be discussed. That jaundice may be persistent in some patients following catarrhal jaundice has also been stated previously by a number of authors.¹⁻⁸ Studies of the plasma bilirubin concentration confirming this statement have been recorded.⁵⁻⁸ In addition, impairment of bilirubin excretion after administration of bilirubin has been described by Soffer and Paulson,⁹ Kalk,^{5, 6} and Kornberg.⁸ The results of the present study confirm these earlier findings. Our observation that abnormally high plasma bilirubin values persisted for years in 25 per cent of this series indicates a higher incidence of chronic mild impairment of hepatic function following catarrhal jaundice than has been generally believed to exist. The fact that impairment of bilirubin excretion is not infrequently demonstrated by the bilirubin-excretion test following catarrhal jaundice, even when there is no chronic hyperbilirubinemia,^{8, 9} indicates that the incidence of chronic mild impairment of liver function is even higher than demonstrated by the 25 per cent incidence of chronic hyperbilirubinemia in our subjects. This concept is supported by the observation that the distribution of the plasma bilirubin values of the 27 patients who had had catarrhal jaundice but had bilirubin values within the normal range includes an abnormally large number of values in the high normal range (Fig. 1).

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medical attention for symptoms unrelated to hepatic dysfunction.

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DISLOCATION OF THE KNEE JOINT*

A Report of Two Cases

JAMES WARREN SEVER, M.D.†

BOSTON

THIS is a report of 2 cases of dislocation of the knee joint—one an anterior dislocation of the knee and the other a compound posterior medial dislocation.

CASE 1. The patient, a 47-year-old carpenter, was admitted to the Cambridge Hospital on June 29, 1942, shortly after falling 15 feet from a ladder. His right leg was in a Thomas splint, which had been applied by the police. Inspection showed an anterior dislocation of the knee (Fig. 1), with the distal end of the femur causing great pressure on the skin in the popliteal space. An anesthetic was immediately given, and the dislocation was reduced on a Bell

The patient was discharged on August 2, with the leg in the bivalved cast, which was removed on September 1. Following this he began to bear weight on the leg, first with crutches and then with a cane, and got about very well. During this period he received physiotherapy for the development of the quadriceps muscle. On September 15, it was noted that he was walking with a marked toe drop and considerable weakness in the peroneal and tibial groups as well as in the dorsal flexors of the foot. As a result of this condition, a short caliper splint was applied to prevent the drop, with marked improvement in walking. The patient continued his physiotherapy. By October he had considerable improvement, and in November the strength of the dorsal flexors, tibials and peroneals had in-



FIGURE 1. Roentgenograms Showing an Anterior Dislocation of the Right Knee (Case 1).

table without great difficulty. In effecting the reduction a heavy canvas strap was placed around the back of the thigh just above the knee, and traction was applied on the lower leg in the line of deformity, with slight flexion at the same time. Following this, a plaster spica was applied from the toes, with the knee flexed at an angle of 20 or 25°. A check-up x-ray film showed no evidence of fracture and complete reduction. Before the dislocation was reduced, there was some obvious interference with the circulation in the toes, but after reduction the circulation was completely restored. The patient wore the spica from June 29 to July 13, when a new cast was applied from the toes to the groin. At that time there was no swelling of the knee joint, the skin was in good condition, and circulation was satisfactory.

On July 29, the cast was bivalved and the leg was inspected. There was good muscle strength, no swelling of the knee and some active motion in the knee joint. There was no apparent lack of stability, but there was still some evidence of ecchymosis about the knee.

almost to normal. He was still wearing his brace, but in the latter part of November he had improved to such an extent that it was removed. At that time he had excellent strength in the quadriceps and had returned to his work. When last seen on February 5, 1943, the knee showed no evidence of pain, discomfort or instability. There was no evidence of any injury to the semilunar cartilages, nor was there evidence of instability due to injury of the crucial ligaments, that is, undue mobility of the tibia on the femur with the leg extended or the knee flexed. The knee could be fully extended and could be flexed 10° beyond a right angle, and the joint was in excellent weight-bearing position. Full power in the dorsal flexors and other muscles of the lower leg had been recovered, and there was no atrophy.

CASE 2† The patient, a 39-year-old telegraph operator, was struck from behind by an automobile on March 14, 1942, suffering a posterior medial dislocation of the left knee (Fig. 2), compounded into the popliteal space through a 7-cm. wound, with periosteal stripping of the lower end of the femur (Fig. 2), as well as a compound comminuted fracture of the upper third of both bones of the lower right leg. He

*From the Orthopedic Clinic, Cambridge Hospital, Cambridge, Massachusetts. Read at a meeting of the Boston Surgical Society, February 7, 1944.

†Assistant professor of orthopedic surgery, Harvard Medical School; orthopedic surgeon, Cambridge Hospital and Children's Hospital.

†I am indebted to Dr. G. Guy Bailey, Jr., for permission to report this case.

treated for 8 weeks in a plaster cast after reduction of dislocation and repair of the compound wound, and so the dislocation was concerned made a perfect recovery. It took considerably longer to repair the condition of the right leg. It was 4 weeks after removal of the cast before the patient attempted weight bearing on the left leg. With physiotherapy, he made a perfect recovery so far as the dislocation was concerned, and eventually the comminuted fracture of the other leg healed, so that he was able to resume work.

At examination on February 12, 1944, the left leg was straight, with excellent muscle strength and full extension of the knee joint, which could be flexed 10° beyond a right



FIGURE 2. Roentgenogram Showing a Posteromedial Dislocation of the Left Knee (Case 2).

angle. There was slight lateral instability or increased motion in the joint. There was no evidence of any injury to the semilunar cartilages as manifested by swelling, locking or instability, and no pain or discomfort. Furthermore, there was no evidence of instability due to injury to the crucial ligaments. In spite of the extensive injury, no injury to the nerves or vessels had been sustained.

DISCUSSION

In the literature on dislocations of the knee,¹⁻⁷ it is emphasized by the various authors that there is total destruction of various ligaments in and about the knee joint. Injuries to the nerves, particularly the peroneal nerve,¹ due to stretching, is not infrequent. In one case the sciatic nerve was completely severed. Occasional cases of thrombosis of the post-tibial as well as the popliteal artery have been reported,^{1,2} these cases requiring amputation.³ The nerve injury, except for the cases showing complete section, usually healed, as was true in Case 1 of this report.

In discussing dislocations of the knee joints, one speaks in terms of displacement of the lower leg; that is, an anterior dislocation means a forward displacement of the tibia on the femur and so forth. This condition is extremely rare, and Ritter⁴ reports that in 23,000 accident cases in the Reconstruction Hospital in New York, dislocation of the knee joint occurred in only 1 case, and that this was not a complete dislocation. He adds that at the New York Post-Graduate Hospital there were only 3 cases in a long period of years. All the authors speak of the comparative ease of reduction, which, of course, is to be expected considering that all the structures about the knee joint have been torn. In one or two reports open operations have been done to reduce the dislocations, but this does not seem indicated.⁵ Most authors believe that fixation for six or eight weeks, later combined with physiotherapy and sometimes with a knee cage splint, is a better form of treatment. Others believe that passive motions begin in ten days, with early weight bearing at fourteen days, is the proper method. It seems wiser to me to wait until the structures about the knee joint have undergone repair before abusing them by early motion and weight bearing.

The most frequent type of dislocation about the knee is the anterior one, which occurred in 40 per cent of the cases reported. This takes place when the knee is in full extension. Posterior dislocations occurred in 20 per cent and result when the knee is in flexion. Lateral dislocations occurred in 20 per cent, and medial ones in 7 per cent. Which of the two latter occurs of course depends on whether the force is applied from the inner or the outer side of the leg. It is interesting to note that in many cases, even with such a severe injury, a satisfactory, stable and excellently functioning knee joint has resulted.

SUMMARY

Two cases of dislocation of the knee joint are reported, and the pertinent literature is discussed.

321 Dartmouth Street

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BOSTON MEDICAL LIBRARY

Report of the President*

IT IS the privilege of our librarian, Dr. Viets, to give an account of our professional activities, of the state of our collections of books, periodicals and memorabilia and of our services to the medical and lay public. The duty of the president is to make known to the fellows and friends of the Library its physical and financial condition, its needs, its projects and its hopes.

The year 1943, the second of our country's complete preoccupation with a desperate global war, has naturally found the Library striving to maintain its facilities and functions rather than to extend its undertakings in a way that would necessarily be incompatible with the war effort. We have not been hibernating, but our circulation and metabolism have suffered inevitable reduction, from which, when peace reigns again, we shall rally to renewed activity and wider usefulness.

There has been a net gain in our membership of twenty-eight. During the year eight fellows have died, as follows: Dr. Seth F. Arnold, Dr. Charles S. Butler, Dr. C. Macfie Campbell, Dr. Isador H. Coriat, Dr. Charles C. Foster, Dr. Amos I. Hadley, Dr. George A. Leland and Dr. Halbert G. Stetson. The loyalty of many of these men who, though they had retired and probably no longer needed the Library, continued actively to support it merits a word of appreciation. Dr. Foster, for instance, did not let his eighty-seven years serve as a reason for resigning; perhaps he continued to enjoy browsing in the stacks or passing a comfortable hour of reading in the Prince Room. We are proud to record that one hundred and fifty-nine of our members are in active service and that we have done what we could to acknowledge our debt to them by remitting their dues.

In my last annual report was recorded the decision of the Rationing Board to reduce our supply of fuel oil to a point incompatible with a continuance of our activities as a going concern, and our consequent contract with the Boston Edison Company to make suitable installations and supply steam for heating. This conversion was promptly and skillfully made, and the new system has been adequate and satisfactory, but it has resulted in an increase of operating expense due not only to the increased cost of service but also to the loss of \$1100 that we received annually by supplying heat under the old system to the Massachusetts Historical Society. We are grateful, however, that we are warmed and sheltered, and able to pursue our work with no more serious interruptions than practice air-raid alarms.

The financial statement and balance sheet have been examined and approved by highly responsible certified public accountants. Last year our income

from fellowship and membership dues was \$497 less than the year before; this year there has been a further decrease of \$411. Our income from investments, however, shows a gratifying increase of \$624, and our actual operating balance sheet shows a deficit considerably less than the \$1305 recorded a year ago. On the other hand, we have had to charge against capital approximately \$9500 to meet the cost of the conversion to steam heat and of structural alterations and renovations to improve the offices of the Massachusetts Medical Society and its organ, the *New England Journal of Medicine*, and of the *Journal of Bone and Joint Surgery*, which is the official publication of the American Orthopaedic Association. This money has been found in part by a loan secured from a commercial bank and in part by borrowing from the unexpended balance of our own restricted funds—a debt that of course must be repaid with the same fidelity as the bank loan. And mention of our financial debts cannot be dismissed without a reminder that our loan from the Massachusetts Medical Society, while somewhat reduced, still stands at \$19,000.

The corporation and friends of the Boston Medical Library must look more deeply into our affairs than merely to scrutinize the balance sheet of our current operations. Actuated by principles of honorable frugality, the trustees have made both ends meet by the most scrupulously careful budgeting. But the Library is in danger of stagnation unless its resources can be materially increased. Our house is in good condition, but it is unfinished. There is room for five additional tiers of steel stacks that were provided for in the original plans, and lacking which our accessions of books and periodicals are piled in the cellar and in passageways. The periodical room is a barnlike hall with the roughest sort of filing alcoves and furniture. Holmes Hall needs refitting and rearrangement to make it really adequate as a reading and delivery room. But more than anything we need improved service. Our director, Mr. Ballard, although he has done better than Ponce de León in his search for the mythical fountain, cannot be expected to carry his heavy burden indefinitely, and a young man of promise should be working by his side, absorbing his familiarity with the Library and its treasures and his skill in library administration—the fruit of fifty years' experience. Our research librarians and cataloguers should likewise have apprentices. A sum of \$100,000 would take care of the improvements in plant, and an additional income of \$10,000 per year would enable us to lead with authority in the plans already made to correlate and unite the various working collections of medical books in and around Boston in a truly co-operative and mutually helpful way. We

*Read at the annual meeting, March 7, 1944.

t search for and inspire generous donors to help with gifts and to remember us in their wills. In the decision of the trustees of a charitable institution that we recently approached that they must grant our request because we obviously had a constituency to whom we could look for support, we must convince public-spirited citizens that the offerings of physicians are rarely sufficient to enable them to make capital contributions.

There are cheerful things to record, as well as sad. The trustees were touched to be told by the executors of the will of the late Annie G. Farlow, widow of our former librarian and enthusiastic supporter, Dr. John W. Farlow, that she had made an unrestricted bequest to the Library of \$10,000 in memory of her husband. Dr. Farlow's avocation was the Library, and to it he gave without stint services more valuable than money. At his death he bequeathed \$10,000, which was applied to urgent needs. His widow paid for the installation of the elevator and has helped us in other ways, and now posthumously adds another to our reasons for gratitude. The Massachusetts Medical Society and the *Journal of Bone and Joint Surgery* have confirmed their alliance with us and have increased their contribution to our support in return for the enlarged space and improved facilities that we have been able to afford them. The Suffolk District

Medical Society has maintained its generous contribution, adding to the sum specifically due us for entertaining them. The James F. Ballard Publication Fund, which we started last year, has financed the publication of the *Catalogue of the Medieval and Renaissance Manuscripts and Incunabula in the Boston Medical Library*, which has been received with great approval by medical librarians and bibliophiles. It is our hope that this fund may receive constant additions, so that publications based on its treasures may be made by the Library from time to time.

As president I cannot close this brief report without paying tribute to the faithful service rendered by those responsible for the well-being of the Library. The trustees have attended the regular meetings of the Board and of standing committees in spite of exacting duties elsewhere. Of the executive officers, who receive no compensation, the secretary, the treasurer and the librarian must give much time to their work, especially the last, whose activity governs and regulates our whole endocrine system. Our director, Mr. Ballard, and the faithful group of research librarians and cataloguers continue the traditions of many years. They deserve the help and support of the corporation of the Boston Medical Library and of a wider public.

DAVID CHEEVER, *President*

MEDICAL PROGRESS

THE LATE EFFECTS OF TOTAL AND SUBTOTAL GASTRECTOMY*

FRANZ J. INGELFINGER, M.D.†

BOSTON

RESECTION of the human stomach, particularly of the distal half, has become a practical surgical procedure that carries a remarkably low mortality rate. In some clinics, gastric resections for malignant tumors are attended by a mortality rate of less than 10 per cent, whereas those carried out for benign lesions have a mortality risk of only 1 to 3 per cent.¹⁻⁶ It is therefore not surprising that gastrectomy is being performed with ever-increasing frequency, not only for gastric neoplasms but also in the treatment of peptic ulcers of the stomach, duodenum and jejunum.

In the case of cancer, gastric resection may have to be most extensive, sometimes total. In the case of ulcer, the amount of stomach removed varies with the operator and the particular problem presented by the patient, but many surgeons recommend that the gastric antrum and at

least two thirds of the stomach be removed, under the reasonable conviction that the chances of a recurrent ulcer are decreased by leaving a gastric remnant that has little or no capacity to form free hydrochloric acid.^{3, 6-9} In short, one purpose in undertaking a gastrectomy for ulcer is the suppression of the normal secretory functions of the stomach.

Can man live without a stomach or with a stomach whose functions are grossly impaired? The answer to this question has always been "Yes," but from time to time it is reported that life under such conditions is not invariably normal. In this review, recent evidence bearing on this problem is considered, for the present popularity of gastrectomy warrants an appraisal of any possible late effects that may follow total or subtotal removal of the stomach. The immediate postoperative complications are not discussed, nor does this review deal with the undoubted efficacy of gastrectomy in the treatment of gastric neoplasms and of

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.
†Assistant professor of medicine, Boston University School of Medicine.

many peptic ulcers. So far as possible, only those effects that can be directly ascribed to resection of gastric tissue are reviewed, but it is probable that some of the symptoms for which gastrectomy has been blamed have actually been caused by post-operative ulcer, gastritis or jejunitis. Allowance must also be made for the fact that many of the data presented by various authors have not had the benefit of a careful statistical analysis, as has been recommended by Hollander and Mage.¹⁰

CLINICAL OBSERVATIONS

Among those patients who have undergone gastrectomy, a clear majority find their mode of life unaffected by the fact that half or more of the stomach has been removed. On the other hand, many patients find it difficult to gain weight, some suffer from postcibal distress, and a few are subject to diarrhea. In a series of 104 patients with subtotal gastric resection, Church and Hinton¹¹ found that 47 per cent lost, 39 per cent gained and the remainder maintained their weight in a post-operative period that averaged nearly three years. Somewhat similar is the experience of Browne and McHardy,¹² who followed 30 gastrectomized patients for periods ranging from two to eleven years after operation and noted that 20 of these lost weight. Miller,⁵ reporting a series of 173 cases, states that the majority did not gain weight easily, but he records actual weight loss in less than 10 per cent. This figure is more in line with the results reported in earlier series.¹³⁻¹⁵

The value of statistical analysis is exemplified by a paper by Santy and Mallet-Guy.¹⁶ These authors divided their material according to the length of the postoperative period and showed that whereas 50 per cent of the patients followed for one to three years failed to regain their normal weight, only a few of the patients observed over longer intervals experienced difficulty in putting on weight. Furthermore, of the 50 per cent who failed to regain their normal weight, only one third — that is, 17 per cent of the whole group — failed to maintain their preoperative weight.

Total gastrectomy in young animals arrests growth and weight gain,^{17, 18} and even adult animals without stomachs may lose weight¹⁹ or require a higher dietary intake than does the normal animal.²⁰ In man, Farris, Ransom and Coller,²¹ and Joll and Adler²² indicate that maintenance of weight does not present a serious problem after total gastrectomy, but Rekers, Pack and Rhoads²³ observe that patients seldom return to their original weights after total removal of the stomach. It is interesting that appetite may be unimpaired after complete gastrectomy.^{22, 24}

The postcibal distress experienced by some gastrectomized patients follows a fairly typical pattern. Even while the patient is still at his meal, and although his appetite may not be assuaged, a marked

sensation of epigastric pressure, distention or fullness develops that prevents him from taking another morsel. Nausea may accompany the symptoms, and occasionally weakness, dizziness, perspiration and palpitation occur within an hour after the meal. To relieve his distress, the patient may belch, induce vomiting or assume certain positions that he has discovered to be effective in mitigating his symptoms. The incidence of a persistent postcibal symptom complex following subtotal or total gastrectomy is probably about 10 per cent,^{11, 13-15} although reports on this point vary. A rather dark picture is drawn by Jordan,⁵ who found that abdominal symptoms occurred post-operatively in 13 of 20 patients operated on for severe duodenal ulcer, in 18 of 41 operated on for bleeding ulcer and in 8 of 12 operated on for stomal ulcer. This series, however, includes ulcer recurrences and other complications. In discussing Jordan's paper, Mateer²⁵ states that after subtotal gastrectomy 14 per cent of his patients suffered from mild and 4 per cent from severe symptoms that could not be ascribed to ulcer recurrences. Of Browne and McHardy's¹² 30 patients, 16 complained of dyspepsia. On the other hand, only 4 of the 74 patients followed by Vitkin²⁷ had epigastric complaints. Three fourths of 113 patients observed by Weissenborn²⁸ were absolutely free of symptoms, about 20 per cent had mild distress, and only 5 per cent had symptoms that interfered with their daily routines. In general, failure to gain weight is particularly noticeable in the group of patients complaining of gastrointestinal symptoms, but the converse does not hold; many underweight patients are completely symptom free.

Frank diarrhea with cramps has been reported as a sequel to gastrectomy,^{12, 29} but it is not very frequent. Many patients, however, find that their stools are soft or even mushy following the operation.

It is emphasized by many writers that the symptoms that can be ascribed to total or subtotal gastrectomy tend to decrease in frequency and intensity as the interval between the operation and the follow-up observations lengthens. Much of the distress present during the first postoperative year tends to disappear subsequently. This improvement is brought about partly by the patient's realization that he must avoid large meals and that he can get along comfortably on six small meals a day. An equally important cause for improvement, however, is the capacity of the gastrointestinal tract to adjust itself to new conditions.

GASTROINTESTINAL MOTILITY

After subtotal gastrectomy, the normal motor functions of the stomach and upper intestines are deranged. Fluoroscopic observations reveal that in some cases material leaves the gastric stump with difficulty, but much more frequently the con-

medium enters the intestine with such rapidity the term "dumping stomach" has been used under these conditions. In an attempt to lessen subsequent motor disorders, many modifications of the method of gastric resection have been proposed, and a considerable argument has developed in the European literature concerning the relative advantages of the Billroth I and Billroth II operations. No conclusive evidence, however, has as yet been presented that one type of operation alters normal gastrointestinal motility less than does the other.²⁷ As will be indicated later, the gastrointestinal tract makes functional adjustments irrespective of the initial surgery, and other factors include the exact size and position of the stoma in determining the rate of gastric evacuation.

In the average patient who makes a good recovery from a subtotal gastrectomy, roentgenologic examination of the gastric remnant shows that this may be somewhat atonic in the early postoperative period, but subsequently it becomes small, appears to exhibit a high degree of tone and is often without a gas bubble.^{14, 16, 27} Ingested barium enters the small intestine rapidly, so that the gastric emptying time is usually much less than that of the normal stomach.^{15, 30} In time, however, the capacity of the gastric stump increases, a process that is effected by elongation of the greater curvature, the gas bubble reappears, and the stomach again assumes some of its reservoir functions. The partially resected stomach sometimes exhibits peristaltic waves,^{27, 31} but in other cases peristalsis is not seen,³² and the general motility pattern tends to be abnormal.¹⁵

Eventually, gastric emptying may occur intermittently and rhythmically, a phenomenon that has suggested to some that a new sphincter is formed by the gastric muscle that adjoins the stoma.^{14, 30} Schindler³³ states that the stoma, as seen through the gastroscope, usually appears patent and rigid, but that in 4 out of 41 patients who had undergone resection for ulcer a rhythmic, pyloruslike activity of the sphincter was seen. Most observers do not believe that a new sphincter forms at the site of the stoma, Vitkin²⁷ maintaining that the stomal aperture is opened and closed by the efferent jejunal loop.

Immediately distal to the anastomosis, the small bowel may dilate and form small accessory reservoirs in which the intestinal content pools before being transported farther down the intestine. Particularly if the gastric remnant is small or if total gastrectomy has been performed, jejunal reservoirs may become large and permanent.²³ Beyond these dilated areas, motility of the small intestine is said to be essentially normal,^{21, 23} or at least the contrast meal reaches the cecum and leaves the small bowel at a normal rate. In the growing monkey, however, puddling and dilatation occur in the lower small intestine after total gastrectomy.¹⁵

Unfortunately, the adjustments of the alimentary canal to subtotal gastrectomy do not proceed smoothly in all patients. Irregular or delayed emptying of the gastric stump may be marked, particularly in the early postoperative period. When emptying is delayed, the usual tendency is to focus all attention on the stoma in an effort to ascertain whether it is too narrow or is improperly placed, or whether there is some mechanical defect in its proximity.³⁴ The fact that many a so-called "nonfunctioning" stoma appears patent when the patient is reoperated on presented somewhat of a riddle until Ravdin and his associates^{35, 36} showed that hypoproteinemia may retard gastric evacuation, both through the pylorus or through a gastroenteric anastomosis. Since then the explanation of hypoproteinemia has been readily invoked to account for many postoperative disorders of gastrointestinal motility, although the evidence for hypoproteinemia may be quite meager. Hypoproteinemia undoubtedly can exert a marked influence on motility,^{37, 38} but other factors are at play, as indicated by the studies of Chauncey and Gray,³⁹ who could not correlate the level of the serum proteins and the rate of gastric emptying through a stoma.

The overemphasis that has been placed on the stoma in explaining abnormal gastrointestinal motility after gastrectomy can be ascribed to the concepts that have been held concerning the emptying mechanism of the normal stomach. In these concepts, the role of the pylorus has occupied a dominant position. Quigley,⁴⁰ however, has shown that in dogs the role of the pylorus is secondary and that gastric evacuation is chiefly controlled by the gastroduodenal pressure gradients. A few observations obtained by Abbott and his collaborators⁴¹ suggest that the same conditions obtain in man. It follows that poor gastric evacuation after subtotal gastrectomy in some cases has nothing to do with the stoma but is produced by a flattened or reversed gastroenteric pressure gradient.

The effect of certain foods on the motility of the upper gastrointestinal tract illustrates the role played by pressure gradients. When fats, hydrochloric acid or hypertonic solutions enter the intestinal loops distal to the anastomosis, the resected as well as the normal stomach exhibits delayed emptying.^{30, 42} This delay, it is now known, is produced by relaxation of the gastric musculature, not by sphincteric contraction. The consequent fall in intragastric pressure may be accompanied, in the case of gastrectomy, by a rise in intraenteric pressure, probably brought about by one of two mechanisms. Either the sudden influx of food activates the motor activity of the small intestine,^{32, 42} or the volume of the intestinal contents is rapidly increased by an outpouring of enteric juices, which take over the diluting functions normally carried out in the stomach.⁴³ The net result of these pres-

sure changes is a flattening of the gastroduodenal or gastrojejunal gradients, with delayed gastric evacuation. To prove that abnormal gradients account for some of the disorders usually ascribed to a defective stoma, better devices for recording intraenteric pressures are needed, but Ravdin, Royster, Riegel and Rhoads⁴⁴ find the indirect evidence strong enough to state: "The feeding mixture should not contain too much fat, for even though the mixture is placed in the jejunum gastric emptying will be delayed. Failure to recognize this fact has greatly increased the time of convalescence of many patients."

The incidence of functional disorders of gastrointestinal motility after gastrectomy is hard to compute. In the first few months after operation, such disorders are doubtless quite prevalent, and they, as well as mechanical stomal defects, should be considered as possible causes of improper gastric evacuation after partial gastrectomy. The edema of hypoproteinemia, if present, may partially occlude the stoma, but it also produces a serious derangement of all gastrointestinal motor functions.^{36, 38} With the aid of proper dietary management, functional disorders tend to subside during the first postoperative year, and subsequently they are encountered infrequently. Among 62 long-standing but poorly functioning gastroenterostomies — not gastrectomies — of various types, Eusterman, Kirklin and Morlock⁴⁵ found that only 6 could be ascribed to abnormal function.

The question naturally arises whether disorders of gastric emptying are particularly prevalent among those patients who experience postcibal distress after gastrectomy. Since the sudden inflation of a balloon in the duodenum often produces epigastric distress, nausea and giddiness,⁴⁶ some hold that these complaints occur after gastric resection because ingested food rapidly enters and distends the small bowel, particularly if the capacity of the gastric remnant is small or if total gastrectomy has been performed.^{47, 48} This theory is compatible with the facts that the postcibal symptoms tend to subside during the first postoperative year and that during the same time new reservoirs are being created, either by enlargement of the gastric stump or by chronic dilatation of the upper small bowel. On the other hand, if the gastric remnant empties very slowly because of some mechanical or functional disorder, it is possible that symptoms of epigastric distress and fullness after eating are produced by abnormal intragastric tension. It must be admitted, however, that the rate of gastric evacuation after subtotal resection, as judged by roentgenologic observations, and the incidence of postcibal symptoms shows, at the most, a weakly positive correlation.^{15, 16} Possibly functional disorders that are induced by the ingestion of certain foods are not evident after suspensions of barium sulfate are taken by mouth.

ABSORPTION

Previous reviews^{49, 50} on the effects of gastrectomy on absorption indicate that fat absorption is sometimes impaired, that fecal loss of nitrogen is excessive in a few scattered cases, but that the absorption of carbohydrates, so far as can be determined by available methods, is not decreased. Glucose administered intravenously is followed by a normal tolerance curve,²¹ but the oral test yields a curve that shows certain deviations from the normal.^{21, 32, 47, 51} In the gastrectomized patient, the blood-sugar level undergoes a steep rise, achieves a high peak and then drops rapidly to levels that may be definitely hypoglycemic. This curve probably depends on the facts that the resected stomach has little capacity to act as a reservoir and that the whole test dose enters the small intestine rapidly and is quickly absorbed. A strong stimulus is thereby exerted on the pancreas, which elaborates sufficient insulin to carry the blood-sugar to abnormally low levels after the absorption of glucose is completed. The secondary hypoglycemia may account for the weakness and perspiration experienced by some gastrectomized patients after taking a meal,³² but opinions on this point differ.⁴⁷

Intestinal digestion of protein apparently proceeds quite rapidly, even in the relative absence of gastric juice,⁵² and oral glycine-tolerance tests indicate that amino acids are readily absorbed by patients with gastric resections.⁵³ In harmony with these observations is the fact that an abnormal loss of fecal nitrogen is most unusual in patients with subtotal gastrectomies. After total gastrectomy, Emery's⁵⁰ dogs showed some fecal loss of nitrogen, but only 1 out of 4 carefully studied human subjects with total gastrectomy suffered from an increased nitrogen output in the stools.^{21, 23} Rekers, Pack and Rhoads²³ believe the nitrogen lost in this case to be of dietary origin, but there is considerable evidence that any process that increases the bulk of the stools may cause an increased fecal excretion of endogenous nitrogen.^{54, 55}

Of the various processes of absorption, that of fats appears to be the one most easily affected by gastrointestinal disorders of all types. Earlier reports of steatorrhea after gastrectomy are found chiefly in the European literature, but recent work on this problem has been carried out in this country by Rhoads and his associates.^{23, 56} These authors report that normal subjects on a diet of 80 gm. of fat a day lost 2 to 6 gm. of fatty material daily in the stools. In 3 patients with total gastrectomies, however, the fecal lipid loss was 11 to 23 gm. a day, although the daily fat intake was only 40 gm. The degree of steatorrhea was not relieved by giving bile salts, Lipocac or intrinsic factor (Ventriculin), nor did it appear to depend on a lack of gastric chyme, a lack of reservoir function or an increased intestinal transport. In 2 of the 3 patients, however, the giving of excess protein by mouth appeared to

improve fat absorption, and in 1 patient steatorrhea as reduced by the oral administration of pancreatic enzymes.

The improvement attending the exhibition of pancreatic material caused Rekers, Pack and Rhoads²³ to suggest that gastrectomy may somehow interfere with pancreatic function. The pancreas has previously been suspected of being responsible for post-gastrectomy steatorrhea, but conclusive evidence on this point has been difficult to obtain. After gastric resection, the duodenal contents is said to contain normal amounts of trypsin and diastase⁵⁷ and urinary diastase is not significantly changed.³² Atoxy-resistant lipase in the serum, believed to be specific for lipase of pancreatic origin,⁵⁸ is reported to be increased in one series of gastrectomies⁵⁹ and not changed in another.³² Santy and Mallet-Guy¹⁶ state that a rather constant production of pancreatic lipase is stimulated in the normal subject after intraduodenal instillation of hydrochloric acid, but that the response in gastrectomized patients is extremely variable and unpredictable, even if the same subject is repeatedly tested. They therefore conclude that gastrectomy disorganizes the mechanisms that control the flow of the external pancreatic secretions. In evaluating contradictory reports on the effects of gastrectomy on pancreatic function, it is well to remember that the determination of pancreatic enzymes is difficult and often unreliable.

After total gastrectomy for cancer, prothrombin levels may not return to normal, but this abnormality cannot be ascribed to faulty absorption of the fat-soluble vitamin K, for even injection of the vitamin may not affect the low prothrombin levels.²⁴ When growing monkeys are gastrectomized, the serum calcium and phosphorus may be diminished and bony changes suggestive of rickets may develop, even though vitamin D is given.¹⁷ In the past, Ivy²⁰ has ascribed disturbances in calcium metabolism in gastrectomized animals to a lack of gastric secretions and to changes in the acid-base equilibrium, but his recent work with growing monkeys suggests that absorption of the fatty vitamin D in these animals may be deficient.

ANEMIA

No doubt exists that the normal stomach, in the digestion of beef muscle, forms some substance that relieves pernicious anemia,⁶⁰ but, after total gastrectomy, this disease does not appear in laboratory animals and occurs extremely rarely in man.^{20, 61-63} Meulengracht⁶⁴ believed that he held the answer to this apparent contradiction when he demonstrated that in the pig the pylorus and the duodenum, not the fundus, contain the antianemic intrinsic factor. Subsequently, however, Meulengracht⁶⁵ was surprised to find that the stomach of patients dying of pernicious anemia showed extensive atrophy of the fundus and a normal ap-

pearance of the pyloric glands. The fallacy of Meulengracht's work lay, as Fox and Castle⁶⁶ showed, in applying his results in pigs to man; in the human stomach, the intrinsic factor is found principally in the fundus. The puzzle therefore still persists: Why do not patients with gastrectomies, particularly those with total gastrectomies, develop pernicious anemia?

As a matter of fact, a small number of patients do. In 1941, Meyer, Schwartz and Weissman⁶⁷ collected 54 cases of what they considered to be authentic cases of pernicious anemia following total gastrectomy. Since then another case has been reported,⁶⁸ but this case and others reported in the past have not had the benefit of a careful study such as Meyer and his associates devoted to their case. Before one can assert that true pernicious anemia occurs as a sequel to gastrectomy, control periods during which the patient receives extrinsic factor, reticulocyte counts before and during liver therapy, adequate follow-up periods and possibly even bone-marrow studies are necessary. Even if the evidence for pernicious anemia is unequivocal, the possibility still exists that some of the cases of pernicious anemia associated with gastrectomy are merely the result of coincidence.

Many patients and animals with gastrectomies do suffer from anemia, but this is usually of the normocytic and the normochromic^{23, 24} or hypochromic variety.^{21, 62, 69} The work of Dragstedt and his associates^{70, 71} indicates that the gastrectomized dog remains anemic on a stock diet but responds well when given excess iron by mouth. Many post-gastrectomy anemias also respond to ferrous sulfate,^{21, 62} but some remain refractory to both iron and liver.^{23, 62} Although parenteral liver extract is recommended for treating post-gastrectomy anemias,⁴⁸ iron is apparently more valuable, either given alone or in conjunction with liver extracts. In addition, proteins and vitamin B complex and its specific fractions, such as riboflavin,⁷² may also have to be given to excess if anemia after gastrectomy is to be prevented.

Petri and his associates^{15, 73} believe that gastrectomy in young swine is followed by a symptom complex closely similar to pellagra. In man, pellagra secondary to gastrectomy has been reported,^{74, 75} but in both cases the condition responded to adequate amounts of niacin (nicotinic acid) and vitamin B complex.

SUMMARY

The consequences of removing portions of the human stomach depend on the nature of the primary disease, the extent of the resection, the surgeon's skill and divers factors that vary with the patient's age, diet and mental attitude. By and large, however, the following statements can be made concerning patients who have undergone subtotal or total gastrectomy:

sure changes is a flattening of the gastroduodenal or gastrojejunal gradients, with delayed gastric evacuation. To prove that abnormal gradients account for some of the disorders usually ascribed to a defective stoma, better devices for recording intraenteric pressures are needed, but Ravdin, Royster, Riegel and Rhoads⁴⁴ find the indirect evidence strong enough to state: "The feeding mixture should not contain too much fat, for even though the mixture is placed in the jejunum gastric emptying will be delayed. Failure to recognize this fact has greatly increased the time of convalescence of many patients."

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-THIRD ANNIVERSARY

House of Delegates, May 15 and 16, 1944

THE House of Delegates convened at the Hotel Carpenter, Manchester, on May 15, 1944, at 7:30 p.m., with Speaker George F. Dwinell presiding.

The following members answered the roll call:

The President, *ex-officio*
The Vice-President, *ex-officio*
The Secretary-Treasurer, *ex-officio*
P. R. Hoyt, Laconia (alternate for Benjamin W. Baker)
Richard W. Robinson, Laconia
W. J. Paul Dye, Wolfeboro
Francis J. C. Dube, Center Ossipee
A. C. Johnston, Keene
Richard C. Batt, Berlin
R. N. Jones, Whitefield (alternate for Leander P. Beaudoin, Berlin)
Arthur B. Sharples, Groveton
Arthur K. Burnham, Lebanon
Leslie K. Sycamore, Hanover
Howard N. Kingsford, Hanover
Donald M. Clark, Peterborough
Stillman G. Davis, Nashua
R. E. Biron, Manchester
Deering G. Smith, Nashua
Clinton R. Mullins, Concord
William P. Clough, Jr., New London
Gerard Gaudreault, Concord
Willard C. Montgomery, Epping
Harry B. Carpenter, Portsmouth

Fred Fernald, Nottingham
Roland J. Bennett, Dover
George G. McGregor, Durham
B. Read Lewin, Claremont
Donald G. Moriarty, Newport

The Speaker declared a quorum present, and appointed the Credentials Committee as follows: Drs. Dube (chairman), Carpenter and Lewin. Dr. Dube reported that the credentials were in order.

The Speaker appointed the Committee on Officers' Reports as follows: Drs. Mullins (chairman), Smith and Montgomery. He appointed the Committee on Communications and Memorials as follows: Drs. Kingsford (chairman), Sharples and Bennett. To the Committee on Nominations, he appointed Drs. Dye (chairman), Robinson, Burnham, Clark and Bennett.

On motion duly made and seconded, it was voted to omit the reading of the previous minutes, because of the publication of the proceedings.

On motion duly made and seconded, it was voted to dispense with the reading of the reports of the councilors, since they will be published in the proceedings.

About 30 per cent of the patients do not regain their normal weight, and some do not regain their preoperative weight.

About 10 per cent suffer from symptoms soon after taking a meal, particularly if the meal is large. These symptoms consist of epigastric distress and pressure, belching, nausea and weakness.

Some patients have soft stools, but very few suffer from persistent diarrhea.

The gastric remnant, which is at first small, gradually enlarges and resumes some of the reservoir function of the stomach. If the gastric remnant is extremely small, the small bowel dilates to form reservoirs near the anastomosis.

Even if the stoma is anatomically perfect, gastric evacuation after subtotal resection may be delayed by functional disorders.

The glucose-tolerance test shows a rapid rise in blood sugar, followed by a fall that may reach hypoglycemic levels. In a few cases symptoms occur during the hypoglycemic phase.

Carbohydrates and proteins are usually adequately absorbed, but some impairment in the absorption of fats may occur.

Pernicious anemia is an extremely rare sequela, but a normochromic or hypochromic anemia is not infrequent.

A nourishing diet, taken frequently in small quantities and fortified with vitamins and iron, often alleviates some of the complications of gastrectomy.

Symptoms and various motility disorders, which may be prominent during the first postoperative year, subsequently tend to correct themselves spontaneously.

Even when the undesirable sequelae of gastrectomy are marked, they rarely interfere with the patient's ability to work, and practically never are they so dangerous or distressing as the disease for which the gastric resection was undertaken. Hence the fact that these sequelae may occur cannot be considered in any sense as a contraindication to gastrectomy in adults. In the rare cases in which resection has to be considered in a growing boy or girl, it may be wise to limit the extent of the resection.

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I asked each county society to have its members contribute \$1 apiece to the National Physicians' Committee. During 1943, \$191.00 was received from the several counties, as follows:

Carroll County	\$13.00
Cos County	36.00
Drafton County	75.00
Merrimack County	1.00
Rockingham County	38.00
Strafford County	28.00

In accordance with your directions the Committee on Medical Economics, with the assistance of the three officers of the Society and of Mr. Sulloway, formulated a plan for a medical-service corporation. Two special meetings of the House of Delegates were held to consider this plan in it developed, one in September and another in November. The Committee on Medical Economics will give you the intimate details in the report that they are making at this meeting.

Several members of the Society have discussed the Wagner Bill before county medical societies, Rotary Clubs and other organizations and have emphasized the fact that the Society has expressed its opposition to this plan for socialized medicine. The Wagner Bill will probably come to the fore in Washington within the next few months. It is still a very definite threat to the present system of the practice of medicine.

We must watch carefully House Bill 352, which was introduced into the New Hampshire Legislature at its recent special session and which was referred, without discussion, to the General Court, which assembles next January. This is a bill "relating to Sickness and Non-Industrial Accident Compensation." It is apparently a slightly modified Wagner Bill that is to be administered not by the federal government but by the State of New Hampshire.

In the several county societies during the past year there has been animated discussion of the Emergency Maternity and Infant Care Program for the families of servicemen, which was promulgated by the Children's Bureau in Washington. This matter was taken up at our meeting a year ago but no definite recommendation was made. A motion was carried that the "House of Delegates consider the Government plan for the payment of hospital and medical care of servicemen's wives at the time of delivery." It was pointed out that many of these patients were able to pay more than the \$35 fee that is provided by the Government, and a suggestion was made that the Government pay this money directly to the patient and that the doctor arrange a suitable fee in each case as he would with other private patients. It is doubtful, however, whether the Children's Bureau will accede to any such suggestion. In California the state medical society has rejected the plan of the Children's Bureau and has voted to treat these women as service cases.

Here in New Hampshire the present status of this program has been summarized as follows:

By and large our physicians are not enthusiastic about the program.

The following are the reasons for the reluctance; the first is the reason most frequently given:

The great fear that this program is an entering wedge for some type of government-controlled medicine.

The seemingly dictatorial way in which this program has been set up; the physician must accept the patient at the fee established by the program and cannot further charge the patient. There is no financial investigation, regardless of the financial status of the patient.

The over-all fee of \$35, which is regardless of the complications that may arise. This fee was set by the Maternity and Infancy Committee of the New Hampshire Medical Society. No state has a fee of more than \$50, and that is the maximum allowed by the Children's Bureau. Maine, New Hampshire and Vermont, comparable states, have a fee of \$35. Massachusetts has a fee of \$50. Physicians cannot understand why cases should not be treated individually. There is the fear that if such a program were here to stay, the physicians would be limited to \$35 and people would begin to think that that was all an obstetric case was worth.

However, most physicians doing obstetrics are participating in this program even though some of them may not be in accord with it, for several reasons:

Pressure from patients or public opinion.

This is an "all-or-none" program and takes care of both hospital and medical bills; if the physician does not sign the application blank, the patient cannot get hospitalization, so the physician, rather than penalize the patient, signs the blank and accepts the patient. This kind of regulation puts pressure on the physician to sign the application. Physicians object to this kind of pressure.

It should be noted that during the coming year the Children's Bureau is asking for seven prenatal examinations of the mother under the present fee schedule; that it is authorizing additional payment for "major non-obstetric surgical operations needed during pregnancy and six weeks postpartum for illness not attributable to pregnancy" at a rate not to exceed a total of \$50 for preoperative, operative and postoperative care; and that it is authorizing additional payment during pregnancy and six weeks postpartum for the home or hospital treatment of "intercurrent conditions not attributable to pregnancy which do not require major surgery." For this care the fee is not to exceed \$12 for the first week of illness and \$6 a week for subsequent weeks of illness. Similar authorizations with the same fees are made for an infant during its first year.

I have asked the Committee on Maternity and Infancy to consider this plan again at the present session and to advise whether or not members of this Society should continue the service under the present arrangement.

Because our program is crowded we have omitted the usual president's address and the report of the trustees. The report of the trustees will, however, be printed in the *New England Journal of Medicine* in a month or two and will be incorporated in the *Transactions* next year.

CARLETON R. METCALF, *Secretary-Treasurer*

On motion duly made and seconded, it was voted that the report of the Secretary-Treasurer be referred to the Committee on Officers' Reports.

Dr. Mullins, chairman of the Committee on Officers' Reports, then spoke as follows:

The Committee on Officers' Reports wishes to congratulate the Secretary-Treasurer on his successful attempt to curtail expenses. We recommend that the contribution to the Benevolence Fund be suspended for this year. The possibility of making this up later by a transfer from the General Fund is suggested. It is thought that the funds for the *New England Journal of Medicine* should be continued, since it serves a rather important purpose. The other suggestions as to Maternity and Infancy are dealt with in the respective committee reports.

Dr. Peters moved the adoption of this portion of the report, and this motion, duly seconded, was carried.

Report of the Committee on Maternity and Infancy

This is the tenth year of the study of maternal and infant deaths.

MATERNAL DEATHS

There were 24 maternal deaths in 1943. There were 9797 live births, thereby giving a maternal mortality of 2.45 per 1000 live births. This may be compared with the figure for 1942, when there were 15 maternal deaths and 9399 live births, a maternal mortality of 1.6 per 1000 live births.

These 24 maternal deaths have been classified according to the *International List of Causes of Deaths* as follows:

The secretary-treasurer, Dr. Carleton R. Metcalf, presented his report, as follows:

MEMBERSHIP, DECEMBER 31, 1943

PAID

Belknap County	23
Carroll County	13
Cheshire County	20
Coos County	25
Grafton County	53
Hillsborough County	104
Merrimack County	57
Rockingham County	51
Strafford County	29
Sullivan County	12
Not in county society	3
	<hr/> 390

UNPAID

Affiliate members	25
Honorary members	6
Members in service	114
	<hr/> 145
	<hr/> 535

The total membership on December 31, 1942, was 551.

FINANCIAL STATEMENT

RECEIPTS

January 1, 1943 — balance forward	\$248.12
Belknap County	168.00
Carroll County	90.00
Cheshire County	126.00
Coos County	168.00
Grafton County	318.00
Hillsborough County	612.00
Merrimack County	366.00
Rockingham County	306.00
Strafford County	168.00
Sullivan County	78.00
Net receipts, 1943 annual meeting	14.99
Cash received at annual meeting	56.00
Members not in county societies	24.00
Refund (Cancer Commission)	9.20
Interest on bonds (received from trustees)	37.50
Women's Auxiliary	25.00
Donations to National Physicians' Committee	191.00
Full subscriptions to <i>New England Journal of Medicine</i>	12.00
General Fund (for Procurement and Assignment)	359.66
General Fund (for Wagner Bill, Blue Shield and general expenses)	1000.00
	<hr/> \$4377.47

EXPENDITURES

<i>New England Journal of Medicine:</i>	
Journals	\$495.11
Full subscriptions	12.00
Transactions	479.41
Carleton R. Metcalf (salary)	400.00
Printing	61.00
Envelopes and stamps	39.67
Eagle and Phoenix Hotel Company (committee lunches)	78.40
Halftone cuts	30.85
Clerical work	163.00
Telephone and telegraph calls	42.03
Mimeographing	26.25
Gold medal	16.75
Frank J. Sulloway (retaining fee, 1941 and 1943)	200.00
Dr. Hsieh (fee as guest speaker)	75.00
Lee and Cope (expenses of guest speakers)	9.09
George C. Wilkins (Cancer Committee)	50.00

Harris E. Powers (expenses at Congress of Industrial Health)	129.62
Deering G. Smith:	
Medical Preparedness expenses	359.66
Dues collected at annual meeting	14.00
Expenses at American Medical Association meeting	141.55
Merrimack Co. and Center district societies (dues collected at annual meeting)	28.00
Leander P. Beaudoin (dues collected at annual meeting)	7.00
Frederic S. Gray (dues collected at annual meeting)	7.00
Benevolence Fund:	
Interest on bonds	37.50
Women's Auxiliary	25.00
\$1.00 per each paid member	404.00
National Physicians' Committee (donations):	
Coos County	36.00
Carroll County	13.00
Grafton County	75.00
Merrimack County	1.00
Rockingham County	38.00
Strafford County	28.00
Madeline A. May (stenographer at annual meeting)	167.60
Blue Shield and Wagner Bill (expenses of meetings and luncheons)	412.00
Mechanics Bank (service charges)	1.60
Flowers (funeral of Mrs. Dennis E. Sullivan)	5.00
	<hr/> \$4109.00
	<hr/> 268.40
Balance, January 1, 1944	<hr/> \$4377.40

The Benevolence Fund on December 31, 1943, amounted to \$2572.78. Of this amount the principal was \$2081.8 and the accrued income \$490.83, part of which was from interest on United States bonds. During the past year we have received \$25 for this fund from the Women's Auxiliary of Merrimack County.

Our receipts have again been curtailed because members who are in the Service do not pay dues and because we have increased the allotment for the Benevolence Fund to \$1 from each member. We have had to draw on the General Fund to make up this deficit. We could decrease our expenses a little for the coming year, but there are on two items in our budget that would make an appreciable difference if they were eliminated. The first item is the *New England Journal of Medicine*. The *Journal* is sent to each member once a month and costs the Society between \$400 and \$500 annually. The second item is the Benevolence Fund. According to a vote of the House of Delegates this fund is to accumulate until it reaches \$10,000. The interest from the fund may then be used to help needy members of the Society. It will be several years, therefore, before this fund becomes effective, and even then the available interest each year will be relatively small. You may wish to discontinue the annual allotment toward this fund for the duration of the war.

We have already economized in our expenses by eliminating a donation of \$100, which for several years was given annually to the Women's Auxiliary, by limiting the annual meeting to one day and by choosing most of our guest speakers from nearby states rather than from distant ones.

Dr. Clarence O. Coburn, of Manchester, died on March 30, 1944. He was a former president of the Society and at the time of his death was a trustee, a councilor from Hillsborough County and a member of the Committee on Tuberculosis.

A year ago the House of Delegates made the following recommendations, which have been carried out:

Fifty dollars was given to the Cancer Committee for its work.

Your president and secretary have conferred with the State Welfare Department, with the result that the fee for old-age assistance cases have been increased. In accordance with the requirement of the federal government, however, the bills of the doctor must still be sent to the recipient and not to the Department.

Why should a physician be forced to sign the application blank, knowing that if he refuses to do so the patient will receive absolutely nothing? That is one outstanding question I have to the program. If the physician does not sign this slip of paper and give the patient the \$35 liberty, she gets nothing.

I see absolutely no reason for this clause's being inserted. A number of pitfalls that a man can find himself under this program is great. I have one case that could have been much worse. A young girl was in her first month of pregnancy, and in the second month she started miscarry. She lived nine miles from the office. I saw her in the middle of the night for two hours, and brought her to the hospital by ambulance. I kept her in the hospital for ten days and took her home myself. I made no house calls. She happened to be a girl who bled every time her period was due. I saw her in the office fifteen times. In the seventh month of pregnancy, she had a premature labor and delivered a 2½-pound infant boy, for some reason or other, made the grade; the mother developed cystitis. We discharged her on the fifteenth day. I had to make three calls to see her after she got home. We kept the baby in the hospital for eight weeks. This particular case could even have been worse, but it is a good example of what we are letting ourselves in for if we sign this blank.

There is also a tremendous difference between putting the program into effect in the cities and in the country towns. Those who practice in the cities can put these patients on ward service, but in the country we have to take care of them and call on them in their homes, no matter where they live.

The whole program has failed in its purpose, too. It would be interesting to note how many obstetricians in the cities are actually taking cases, and how many women are actually getting the care they want. I doubt if many of the obstetricians are taking them. They are going around, hunting for some doctor to take them for \$35, with the result that they get somebody who is not too good an obstetrician.

Dr. Gaudreault said that he was in perfect agreement with Dr. Clough. He thought that the forms could be submitted to the superintendents of hospitals and should be signed by them and that the doctors should be allowed to do what they please. He said that he would much rather deliver a case for nothing than be paid \$35 for his services. He believed that if anyone was willing to sign a paper he should receive at least \$50, as in Massachusetts and several other states. He recommended two different forms — one for the hospital and one for the physician.

Dr. Dube said that the superintendent of his local hospital was seriously disturbed by the whole affair. Apparently some time ago the hospital was offered a lump sum of \$50, but the option was then withdrawn and the hospital was asked to find the per capita cost for keeping a maternity patient. A detailed statistical report was wanted covering the number of patients in the hospital, the number of private rooms, the number of nurses on hand, the exact cost of food per meal and everything else. Apparently the hospital was being offered not over 15 per cent of the per capita cost of the care of the patient. Dr. Dube asked for information from the committee on the matter.

Dr. Smith then read the following extract from his report as delegate to the meeting of the American Medical Association:

The action of the federal government in making funds available for maternity and infant care for the wives and infants of enlisted men was approved and adoption was urged of a plan under which the federal government will provide for the wives of enlisted men a stated allotment for medical, hospital, maternity and infant care similar to the allotments already provided for the maintenance of dependents, leaving the actual arrangements with respect to fees to be fixed by mutual agreement with the wife and the physician of her choice. This action was similar to that taken by the New Hampshire House of Delegates last May. A copy of the resolution was sent to each congressman and each senator urging that a method of making available these funds be changed to an allotment basis. After considerable discussion in the House of Representatives, the proposal was rejected by a vote of 115 to 8.

He spoke as follows:

My feeling is that medical care is no different than the provision of fuel, food and shelter and clothing for the wives and children of the servicemen, and that medical care should be included in the allotments or allowances now given to servicemen. If the allowances, as they are called, are not large enough to take care of the wife and the children when they are sick or when the wife is going to have a baby, they should be increased. They are, as you know, a matter of record, varying according to the number of children a soldier has. If there are no children, the wife receives \$50 a month from the Government; if there is one child, she receives \$80 a month; if there are two children, she receives \$100, and there is an increase of \$20 for each additional child. Of this money, \$22 comes from the soldier's pay and the balance is made up by the Government.

Much as we want to take care of the soldier's wives, why should we do it at a cut rate when the Government is paying the full rate for other essential services?

Dr. Mary Atchison spoke as follows:

I am here neither to defend nor to sell. I feel, however, that the time has come for this controversial subject to be discussed frankly and openly. We in the State Health Department who have been delegated with the job of trying to administer this formidable program find ourselves in the middle, so to speak.

The fact is that funds are made available through the program by an act of Congress for the care of the specific group of individuals, namely, the wives and prospective mothers of servicemen, and up to this date there is no other source of funds for the women.

Medical care, to be sure, is absolutely no longer a luxury; it is a necessity, and it should be so classed as much as is food, clothing or shelter, as Dr. Smith has stated.

If the wife of a serviceman becomes ill with any other condition than pregnancy, no provision is made for her. Therefore, this program is, as designated, an emergency maternity program, and infant care is included in other states. We have been promised that the program is for the duration of the war and for six months thereafter, only. I think we should safeguard our rights in this regard.

I happened to be present at the state health officers' meeting in Washington when this matter was frankly discussed. The state health officers told the Children's Bureau officials exactly what they thought in regard to the manner of administration, the red tape, the requirements and the restrictions imposed in the administration of this program.

By and large, the physicians in New Hampshire have co-operated beautifully. They have given their time. They have, without liking it, given their services, and these have been of the best. We are grateful to you for doing that.

We sent out a bulletin to you before this meeting, and enclosed with it a short explanatory note. The bulletin had a formidable outline. We asked you to read and study it, so that you would know what the proposals or the policies are. We asked you in particular to note Item 4, which describes the services that are available under

	CLASSIFICATION	No. OF DEATHS
147 (<i>d</i>)	Puerperal embolism (during childbirth and puerperium)	5
146 (<i>c</i>)	Hemorrhage of childbirth and puerperium as placenta accreta, post partum	4
146 (<i>a</i>)	" " " " placenta previa with childbirth	2
148 (<i>a</i>)	" " " " " " " " " " h after delivery)	2
149 (<i>b</i>)	" " " " " " " " " " cesarean section	2
146 (<i>b</i>)	Hemorrhage — premature separation of placenta with childbirth	2
147 (<i>b</i>)	Infection during childbirth and puerperium	2
143 (<i>b</i>)	Hemorrhage — premature separation before delivery	1
144 (<i>d</i>)	Toxemia of pregnancy (death before delivery)	1
149 (<i>a</i>)	Accidents of pregnancy — inversion of uterus	1
140 (<i>b</i>)	Abortion with infection	1
148 (<i>b</i>)	Puerperal toxemia (albuminuria and nephritis).	1
Total	24

The committee has reclassified these for the purpose of this report in the following way:

CAUSE OF DEATH	No. of DEATHS
Accidents of pregnancy	6
Puerperal embolism	5
Inversion of uterus	1
Hemorrhage	9
Placenta previa	2
Premature separation	1
Retained placenta	3
Uterine inertia	3
Toxemia (all types)	4
Puerperal sepsis	4
Abortion with infection	1
Total	24

The 14 cases reviewed were listed on the death certificates as follows:

Embolism; endometritis (G6)
Hemorrhage and shock; premature separation of the placenta; death before delivery (G2)
Postoperative shock and hemorrhage; placenta accreta (G3)
Eclampsia; pregnancy with toxemia (G10)
Post-partum hemorrhage and shock; placenta previa complete (G4)
Embolism of lungs (acute schizophrenia) (G24)
Embolism; endometritis (G6)
Toxemia of pregnancy; acute nephritis (G11)
Hemorrhage; placenta previa (G13)
Coronary thrombosis following childbirth (G14)
Premature separation of placenta with shock and hemorrhage (G17)
Post-partum hemorrhage (G18)
Peritonitis and intestinal paralysis following cesarean section (G19)
Eclampsia (G21)

The 10 cases not reviewed were listed on the death certificates as follows:

Inertia of uterus with uterine hemorrhage
Toxemia of pregnancy
Purulent endocarditis; sevelar thrombi; atelectasis of lung; cesarean section
Pulmonary embolism; difficult delivery
Inversion of uterus
Pulmonary embolism; cesarean section
Shock; abruptio placentas; hydrocephalic breech
Cardiac collapse and generalized toxemia; penetration of uterus by piercing instrument; post-abortion uterus
Acute dilatation of stomach due to intestinal obstruction following operative delivery; acute peritonitis
Post-partum hemorrhage

Of the cases reviewed, in Cases G2, G3, G4, G6, G13 and G18 more information was needed in order to classify them. Cases G10, G17 and G21 were classified as due to the fault of the patient; Cases G11 and G24 were unavoidable; and Cases G14 and G19 were probably avoidable.

INFANT MORTALITY

Included in this group are those infants who died under one year of age. There were 420 infant deaths in 1943, giving an infant death rate of 42.9 per 1000 live births, compared with a rate of 33.5 in 1942. The causes of death were as follows:

CAUSE OF DEATH		No. of DEATHS
Deaths occurring during the first day:		
Prematurity		90
Birth injuries		22
Congenital deformities		15
Atelectasis		7
Congenital debility		2
Cerebral hemorrhage		1
Bronchopneumonia		1
Pulmonary emphysema		1
Syphilis		1
Unknown		1
Total		141

Deaths occurring during the first month exclusive of the first day:	
Prematurity	44
Congenital deformities	35
Birth injuries (all kinds)	5
Atelectasis	7
Diseases of gastrointestinal tract (diarrhea, enteritis and so forth)	11
Pneumonia (all types)	11
Hemorrhagic disease of newborn	1
Diseases of thymus gland	1
Congenital debility	1
Acute nephritis	1
Unknown	1
Total	121

Deaths occurring from the second to the twelfth month, inclusive:

Pneumonia (all types, with complications—empyema and so forth)	50
Congenital malformations	23
Gastroenteritis	2
Influenza	1
Whooping cough	1
Pyelonephritis	
Congenital debility	
Birth injury	
Suffocation	
Atelectasis	
Tuberculosis (pulmonary)	
Meningitis	
Cancer of intestines	
Endocarditis	
Otitis media	
Mental deficiency	
Convulsions	
Unknown	
Total	153

The causes of 211 still births were as follows:

CAUSE OF STILL BIRTH		No.
Causes	No.	Causes
Stillborn (cause unknown)	1	
Intrauterine death (cause unknown)	1	
Toxemia	1	
Difficult delivery	2	
Asphyxia neonatorum	2	
Prematurity	4	
Congenital malformations	2	
Premature separation of placenta		
Placenta previa		
Erythroblastosis		
Ruptured uterus		
Total	21	

The committee, with the aid of Dr. Burpee, the consultant, has formed the following recommendations in regard to Emergency Maternity and Infancy Care Program.

- That the physicians of New Hampshire, as a part of their war effort, participate in the maternity program in the future as they have done during the past year.

That the fee for services under this program be increased to \$50 per case.

That the program suggested for additional care of major surgical and medical conditions occurring in course of pregnancy not be accepted. (This recommendation is made because of the difficulty involved in determining the meaning of the term "qualified consultation as demanded under the program.")

That the child-health program be accepted under following conditions:

following conditions:

- The major surgical aid not to be included (a) because of the difficulty in determining the meaning of the term "qualified consultants").
- The aid not to be accepted for illnesses requiring

The medical aid to be accepted for illnesses requiring over two home or office visits. (This plan would eliminate many needless calls on essentially well babies and would avoid a great deal of extra work involved in applying for aid, authorizing the service and approving the records for payment.)

MARION FAIRFIELD, Chair
JOHN J. BOARDMAN
BENJAMIN P. BURPEE, Consul

Dr. Clough then spoke as follows:

I think there is not one of us who is not perfectly willing to do anything we can for servicemen's wives, we are unwilling to have this thing forced down our throats.

By the way there is nothing compulsory about this. The program is accepted by the medical society in principle. If you do not want to participate in it, you can say at you are too busy, that you would like to do it but not. That is your problem.

Dr. Gaudreault remarked that the program still the doctor "holding the bag."

Dr. Atchison replied that under the maximum \$35 the doctor "was holding the bag," and that was a little fairer. She thought that if every-asked himself, "How much do you actually ect?" he would admit that it would be somewhere he vicinity of \$50.

The Committee on Officers' Reports moved that

this program as recommended by the Committee on Maternity and Infancy be accepted. He outlined these recommendations as follows:

That the physicians of New Hampshire, as a part of their war effort, participate in the maternity program in the future as they have done during the past year.

That the fee for services under this program be increased to \$50 per case.

That the program suggested for additional care for major surgical and medical conditions occurring in the course of pregnancy be not accepted.

This motion was duly seconded and was carried with three dissenting votes.

(To be continued)

SE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30351

PRESENTATION OF CASE

First admission. A fifty-nine-year-old housewife entered the hospital because of "heart trouble." The patient had been in apparent good health until about three or four months before entry, when she developed chills, fever, chest pain and cough, diagnosed and treated as pneumonia by her physician. She recovered in about one month, but remained in bed except for about two or three hours daily. About two months before admission she had sudden attack of agonizing, squeezing pain in the chest associated with inability "to catch her breath." She said that she felt as though she were "dying." The pain and dyspnea lasted for five hours and were finally relieved by a hypodermic injection by her physician. From that time on, she had attacks of nocturnal dyspnea occurring two or three times a week, which were relieved by injections, the nature of which is not recorded. She had marked orthopnea, requiring three pillows. One month before entry she developed frequent attacks of nausea and vomiting.

At forty-one years of age, following an episode of polydipsia, polyuria and weakness, she was found to have diabetes. The diet was regulated and she was placed on 4 units of insulin three times a day. Four months before admission the insulin was re-

*On leave of absence.

duced to 4 units twice a day. Since no sugar appeared in the urine, the insulin was not increased during the course of the pneumonia, and one and a half months before entry it was stopped completely without any symptoms. One year before admission she experienced swelling of the ankles, and about six months later was found to have a systolic blood pressure of about 200. The past history was otherwise negative.

Physical examination showed a well-developed but poorly nourished dyspneic woman. The heart was enlarged. The apical impulse was palpable in the anterior axillary line. The sounds were strong, labored and regular. The first sound was clear. No definite murmurs were heard. The aortic second sound was greater than the pulmonic. The liver edge was palpated two fingerbreadths below the costal margin. There was moderate sacral and ankle edema. Ophthalmoscopic examination showed irregular thickening of the arterioles and the silver-wire reflex, as well as a number of small flame-shaped hemorrhages at the branching of the vessels. Foci of old hemorrhage and spots of exudation were present.

The blood pressure was 254 systolic, 100 diastolic. The temperature was 100°F., the pulse 90, and the respirations 20.

Examination of the blood showed a red-cell count of 2,000,000, with 6 gm. of hemoglobin. The white-cell count was 6600, with 60 per cent neutrophils. A blood Hinton test was negative. The urine was slightly cloudy, with a specific gravity of 1.012 and a pH of 7.5; it gave a + + + + + test for albumin but no reaction for sugar, diacetic acid, acetone or bile. One or 2 red cells and 3 or 4 white cells per high-power field were seen in the sediment. A culture yielded *Staphylococcus albus* and colon bacilli. Stool examination was negative.

An x-ray film of the chest showed an enlarged heart whose borders, however, were obscured by fluid in the pleural cavities. The pulmonary markings were prominent. The nonprotein nitrogen was 77 mg. per 100 cc., the protein 4.8 gm., and the

the program. Your Committee on Maternity and Infancy has studied this program with a great deal of care and albeit, after much frank discussion, they do not approve of all of it. It is within our rights to prepare a program, provided you will accept it in principle advising us as to the parts of the program that you think might be workable. We are asking for a ceiling fee for maternity care of \$50, and if this is accepted by you I am almost certain we shall get it. The reason we have not asked for \$50 before is that when the program was first started, the ceiling set by the Bureau was \$35. Gradually, the various states studying the matter reached the conclusion that a maternity case could not be handled for \$35. It was stated that if that was all such a case was worth, the physicians were not going on record as saying that they would lower their standards in order to give a \$35 delivery. So Massachusetts and some of the larger states asked for \$50 and got it. I understand from my colleagues in Vermont and Maine that they are going to do the same.

In the beginning, in such a case as Dr. Clough described, we were not allowed to make any additional provisions. As stated in the bulletin we shall be allowed to pay an additional amount for time and travel on a mileage basis. We do not like these limitations any more than you do. These policies were worked out by the Children's Bureau with its medical advisory committee, which is made up of some of the best minds in the country — representatives of the American Medical Association, obstetricians, pediatricians and men recognized in the field of medicine as the best.

This is a mass-production type of program. It was designed, of course, to fit the United States as a whole. We cannot possibly say that one plan is going to fit the whole situation. From letters that we have received we have assurances that we can use our own judgment.

I want to compliment Dr. Chamberlain for the conscientious manner in which she has tried to administer the program. I am not saying whether or not it should be adopted, but I want you to know that we are constantly aware of the needs of the profession and its problems, and our only purpose is to try to protect its interests so far as a program of this type is concerned.

When this act was passed by Congress there must have been some reason for it, and this was pressure from certain groups. The American Red Cross, all the labor unions and others simply went to Washington and demanded that something be done.

As I understand it, the entire intent of the program is a service to the serviceman and his family.

The matter of the payment of funds to the family was also discussed. It was thought that the most democratic thing to do was to give the patient a sum of money and say to him or her, "Pay your bill." However, we in the Department of Public Welfare, who administer the public-relief moneys, know that the grocer gets paid, the furniture dealer gets paid, the dry-goods store gets paid, but the doctor does not get paid. When the patient gets the money, there is nothing that says, "You must pay the doctor." Human beings are human beings; therefore, from an administrative standpoint, it is much better, in providing services, in order to safeguard everything, that the doctor be paid by an official agency. The official agency is the department that has in it medical personnel. The only reason that the payment is made in this way is that the doctor can thus be sure of what he is getting.

Dr. Mullins asked whether if this program were rejected it would work a real hardship on the women concerned in this state.

Dr. Atchison replied that, although she had no statistics to bear out her statement, the program was needed. The Grenier Field Army Base, for instance, had previously taken care of the Army wives, but had now discontinued this service which meant that the women with the \$50 allotment were put on their own and would have to obtain care. She did not see why the doctor should

"take the rap," since the patients had to pay the hospitals.

Dr. Mullins asked whether the hospitalization part of the infant-care program was connected with the physician's care, and whether the hospital care would still be allowed.

Dr. Atchison believed that the principle was the same, and Dr. Chamberlain said that it was the same setup. Dr. Atchison explained that the intention was that the patient should be assured of medical care of some sort, and of course would get hospital care, too. The hospital would be paid on a per diem ward cost basis, which would vary with different hospitals. This cost was to include diagnostic procedures, x-ray examinations, laboratory fees and what not.

Dr. Dube pointed out that this cost was nearly \$6 a day. Dr. Atchison agreed, and remarked that if a maternity case was complicated, the physician would take a loss, but that if he had 100 cases and the majority of them were normal, he would not fare too badly. She added that, as a matter of fact, many physicians in the rural areas seemed to favor this program more than one would suspect. The city physicians, of course, had a higher overhead and they claimed that \$35 was nothing but that \$50 was a little better. However, in some states the physician got at the most \$15 for a delivery, and even then could not collect it, so that many of them were willing to handle the case on the present basis.

Dr. Clough said that it depended on what type of obstetrics one was practicing. He believed that the price for all should be elevated, not brought down. It seemed to be the accepted attitude that obstetrics was not worth much, but this idea was absolutely wrong.

Dr. Atchison agreed. She added that of course it could not be said that one physician was worth \$100 and another \$25 and still others \$15 or \$50, so that a uniform method was the only possible one for proper administration of payments.

Dr. Dye asked whether women who accept war rate care could have private rooms. Dr. Atchison replied, "No."

Dr. Gaudreault said that he still believed that the doctor and the superintendent of the hospital should both sign the form, and have the doctor free to give the patient the care she needed and still not deny her the privilege of having her hospital care paid for by the Government.

Dr. Atchison spoke as follows:

Under certain conditions under which these services are made available, Dr. Chamberlain and I see a loophole. For instance, these services may be authorized provided similar services are not available. Suppose there is not a service in the hospital and that there is a clinic available in a certain town to which the patient can go. If she so chooses, all right. A wife has three choices under the program, including all types of available facilities. She may not want to go to a clinic, and may prefer a private practitioner and ask for one.

anatomopathological conference that Dr. Richard C. Cabot conducted years ago, when he was handed an abstract of the history on the spot.

It seems reasonable that a diagnosis of pneumonia was made following the episode of chills and fever, chest pain and cough. The next attack of chest pain and dyspnea lasted for five hours. Was it substernal?

DR. BENJAMIN CASTLEMAN: It does not say.

DR. CHAPMAN: The pain was squeezing and constricting, so I suspect that it was substernal.

Hypertension was discovered a year before entry, and the patient had edema of the ankles at that time. On physical examination advanced arteriosclerotic changes were found in the eyegrounds.

According to the laboratory notes the red-cell count was surprisingly low, and it is interesting that the specific gravity of the urine was so low (1.012). When a patient is dehydrated at entry one always looks at the first gravity, because it is of more significance than subsequent tests in the hospital, since the patient is usually given extra fluid. I assume this was an admission specimen.

DR. CASTLEMAN: The specific gravity of the urine is at first 1.012, then 1.010, 1.008 and 1.020.

DR. CHAPMAN: The record states that after eighteen days the patient's condition improved. I am not so impressed with the improvement.

The electrocardiographic changes are more than consistent with left ventricular enlargement; they suggest damage to the anterior wall of the myocardium.

The patient had a potential diabetic background. Her blood sugar was slightly above normal, but not very high. She evidently was diabetic and also hypertensive. I do not see much point in giving 4 units of insulin three times a day, since this is an unnecessary burden to place on a patient. She might have taken one dose or regulated her diet.

A year before admission she developed hypertension and then began to have swelling of the ankles.

She entered the hospital with the story of being well until the sudden onset of chills and fever, the diagnosis of pneumonia at the left base having been made. Pulmonary infarction is often treated as pneumonia because the signs and clinical story are often similar. Since this patient continued to have symptoms, in retrospect one has to consider infarction strongly. The second attack may have been due to more pulmonary emboli. She had changes in the circulation. Linton and his co-workers¹ in a recent publication covering 202 cases of pulmonary embolism and infarction state that 70 per cent occur in the left lower lobe, although most reports, including that of Hampton and Castleman,² name the right lower lobe as the favorite site. I think that is significant. I believe that this patient had an embolus and not true pneumonia.

The next question is, Was this true angina or did she have coronary occlusion with myocardial infarction of the anterior wall? The fact that it lasted five hours suggests that she had infarction. That is too long for angina.

Then she re-entered the hospital and died in uremia. I think that the persistent pneumonia, the persistent hypertension, the persistent edema and the whole clinical story — the gradual going down hill and death in uremia after a long hospital entry — favor the thing that we have been led to suspect, that is, an intercapillary glomerulosclerosis, which has been described by Kimmelstiel and Wilson³ and which happens so often in diabetics. I believe that Dr. Castleman will show us kidneys with deposits between the capillary tufts. Edema is an outstanding clinical feature in these patients. Certainly this woman had edema, and they even used Southey tubes for it. She had pericarditis with a pericardial friction rub. As a routine interpretation we might say that the electrocardiogram showed infarction of the anterior wall with inversion of the T waves and a deep Q₃, with inversion of CF₄ and CF₅. I believe, however, that she did not have an occlusion, because the pericarditis could have produced these changes. In other words coronary occlusion with infarction in the anterior wall can be simulated in all respects by pericarditis, with or without effusion. An excellent paper on that point has just been published by Wolff,⁴ who reported 5 cases seen at the Beth Israel Hospital.

The development of the blowing diastolic murmur does not disturb me. I do not believe that we have to think of aortic regurgitation, because the murmur disappeared when the patient became compensated. I wish that Dr. Butler would comment on the blood chemical findings.

DR. ALLAN M. BUTLER: One gram of ammonium chloride daily had marked effect in producing an acidosis, the carbon dioxide dropping to 13 millimols and the chloride rising to 114 milliequiv. I think that makes sense in a patient who has marked renal damage and hence does not produce ammonia and cannot excrete sodium and chloride differentially. The next time they gave 1 gm. of ammonium chloride four times a day, but only for one day.

I suppose that this patient had marked arteriosclerosis and vascular nephritis. I wonder about the diabetes. She probably had it, but we are given no real evidence except that someone said so.

DR. CHAPMAN: She was given insulin; in other words, someone thought she had it. We do not know how limited the diet was in carbohydrate.

DR. BUTLER: There is no evidence of diabetes in the story given us, and we have to assume that it was present. On the other hand, she was not paying much attention to diet, not taking insulin and not showing much evidence of diabetes.

DR. CHAPMAN: I am interested that she put out 5 per cent of phenolsulfonephthalein dye at the end of

blood sugar 123 mg. The carbon dioxide was 20.6 millimols per liter, and the chloride 103.2 milliequiv. The fluid intake was limited to 1800 cc. She was given 0.011 gm. ($\frac{1}{6}$ gr.) of morphine and 0.2 gm. (3 gr.) of digitalis three times a day for two days and 0.1 gm. ($\frac{1}{2}$ gr.) of the latter daily thereafter, as well as 1 gm. (15 gr.) of ammonium chloride daily. After the second hospital day she was started on protamine zinc insulin, 20 units daily for two or three days.

During the first hospital week she vomited considerably and complained of subxiphoid pain. The vomiting finally stopped. On the seventh hospital day the nonprotein nitrogen was 90 mg. per 100 cc. The protein was 6.0 gm. per 100 cc., with an albumin-globulin ratio of 2. The carbon dioxide was 13.2 millimols per liter, and the blood chloride 113.8 milliequiv. She was given 0.13 gm. (2 gr.) of sodium phenobarbital subcutaneously three times a day. A phenolsulfonephthalein test gave less than 5 per cent excretion at the end of an hour. In the course of the next eighteen days her condition improved remarkably; the carbon dioxide rose to 16.4 millimols per liter, and she was discharged on 0.1 gm. ($\frac{1}{2}$ gr.) digitalis daily and limited fluid intake.

Final admission (one and a half months later). Following discharge the patient failed to follow directions. She was irregular in taking digitalis, drank "lots" of water and did not keep her appointment at the Out Patient Department. She became progressively more dyspneic, with increasing edema and marked orthopnea. Eight hours before admission she developed severe respiratory distress.

Physical examination showed a slightly cyanotic woman in acute dyspnea. The lung bases were dull up to the fifth interspace. Many coarse rales and wheezes were heard throughout. The breath sounds were decreased at the bases. The heart was enlarged to 4 cm. beyond the midclavicular line. A low-pitched early mid-diastolic blowing murmur was heard at the aortic region. A pericardial friction rub was audible at the base. The abdomen was negative. There was marked pitting edema of the ankles, extending to the level of the lower thorax, where only a slight pitting edema was present.

The blood pressure was 210 systolic, 110 diastolic. The temperature was 97.6°F., the pulse 120, and the respirations 30.

Examination of the blood showed a red-cell count of 3,200,000, with 5.5 gm. of hemoglobin. The white-cell count was 6400, with 60 per cent neutrophils. The urine was cloudy, with a specific gravity of 1.008 and a pH of 7.5; it gave a +++ test for albumin and contained a trace of acetone. The sediment had 1 or 2 white cells per high-power field. The nonprotein nitrogen was 140 mg. per 100 cc., and the carbon dioxide 22.3 millimols per liter; the protein was 6.0 gm. per 100 cc., with an albumin-globulin ratio of 1.2. An electrocardiogram showed a

rate of 95. The PR interval was 0.12 second. Slight left-axis deviation was present. ST₁ and ST₂ were slightly depressed, with low inversion of T₁, T₂ and T₃. Q₃ was deep, and the T wave was low in CF₄ and low and inverted in CF₅.

She was given 0.011 gm. of morphine sulfate and two transfusions of 250 cc. of whole blood each. She was also given 0.2 gm. of digitalis for two days, followed by 0.1 gm. daily, 1 gm. of ammonium chloride four times a day (for four doses), followed by 2.2 cc. of Mercupurin intravenously, and daily infusions of 25 per cent dextrose in water.

On the fourth hospital day she vomited several times. The urine continued to remain alkaline and to give a +++ or ++++ test for albumin. The basal rales diminished. The friction rub was still present, but the aortic diastolic murmur could not be heard. The blood pressure was 210 systolic, 100 diastolic. The nonprotein nitrogen was 120 mg. per 100 cc. The carbon dioxide was 20.2 millimols per liter, the chloride 93.3 milliequiv., and the blood sugar 15 mg. per 100 cc. An x-ray film of the chest showed fluid in both pleural cavities. The urinary output was 500 cc. on an intake of 1250 cc.

On the ninth hospital day pitting edema was noted extending to the neck. The pericardial friction rub was heard in the third interspace to the left of the sternum. On the eleventh hospital day 1200 cc. of clear, yellow fluid was withdrawn from the right thorax. The specific gravity of the fluid was 1.005 and it contained 180 cells per cubic millimeter, with 10 per cent red cells, 45 per cent lymphocytes, and 45 per cent monocytes. On the thirteenth hospital day she had severe, acute respiratory distress and considerable discomfort because of severe edema in the legs. Another chest tap, on the fourteenth hospital day, gave 1300 cc. of fluid from the right side and 1100 cc. from the left. The dyspnea improved temporarily but during the following week it increased. On the twenty-third hospital day Southey tubes were inserted in both ankle and thoracentesis yielded 1000 cc. from the right and 800 cc. from the left, with much improvement in the dyspnea. In the next three weeks, however repeated chest taps were necessary. On the forty-ninth hospital day she became nauseated and began to vomit. She had considerable headache. The nausea and vomiting persisted despite atropine. The pericardial friction rub became louder; the nonprotein nitrogen was 108 mg. per 100 cc. The vital capacity was 1300 cc. She continued to get digitalis.

Her condition became progressively worse, and she died on the sixty-third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: Through an error I received the wrong clinical abstract but I shall attempt to discuss this case without having prepared it. In other words, it resolves into the type of

pericarditis, which at the time of autopsy was in the healing stage. There has been a lot of discussion about the appearance of the myocardium in patients with renal failure. Most people believe that there is no definite myocarditis due to renal failure, though Gouley⁶ has stated that there is a characteristic myocardial degeneration.

DR. CHAPMAN: How extensive was the recent infarction?

DR. CASTLEMAN: It was very extensive and certainly not more than a week or two old.

DR. CHAPMAN: Then it could not explain the changes in the electrocardiogram taken sixty days before.

DR. CASTLEMAN: No.

DR. CHAPMAN: They might well have been explained on the basis of the acute pericarditis that he had had at the time.

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The kidneys weighed 250 gm. and showed numerous scars throughout. Microscopically we found the condition that Dr. Chapman predicted. Most of the glomeruli showed extensive hyalinization in such a fashion as to give the tufts a lobulated appearance, the sclerosis being predominantly intercapillary. Many of the peripheral capillaries were patent. This is the characteristic picture described by Kimmelstiel and Wilson.³

DR. BUTLER: How about the small arterioles?

DR. CASTLEMAN: There was a goodly amount of vascular nephritis as well.

The only remnant of the old process in the left lower lung was a fibrous diaphragmatic pleuritis. Unfortunately, sections through the underlying parenchyma were not taken for microscopic examination, so that we do not know whether the lesion was due to an infarct or pneumonia.

REFERENCES

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- 4 Wolf, L. Acute pericarditis simulating myocardial infarction. *New Eng. J. Med.* 230: 422-425, 1944
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- 6 Gouley, B. A. Myocardial degeneration associated with uremia in advanced hypertensive disease and chronic glomerular nephritis. *Am. J. M. Sc.* 200: 39-49, 1940

CASE 30352

PRESENTATION OF CASE

A twelve-year-old schoolboy entered the hospital complaining of pain in the right hip.

The patient had been well until three months before admission, when he slipped and fell on his right hip. He developed pain and limitation of

motion which became progressively worse two to three weeks before admission.

Physical examination showed a well-developed, well-nourished boy in no acute distress. The heart, lungs and abdomen were negative. There was tenderness over the lateral aspect of the right hip, and marked limitation of motion due to spasm and pain.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 100°F., the pulse 85, and the respirations 25.

Examination of the blood showed a white-cell count of 8600, with 71 per cent neutrophils, 22 per cent lymphocytes, 4 per cent monocytes, 2 per cent basophils and 1 per cent eosinophils. The hemoglobin was 12.8 gm. per 100 cc. The urine was normal. A blood Hinton test was negative.

Anteroposterior stereoscopic films of the pelvis showed destruction of the right ilium along the entire region of the right sacroiliac joint (Fig. 1). The process appeared to extend well into the ilium and to involve the medial half of the iliac crest. The joint itself and the sacral side of the joint did not appear to be involved. There was a soft-tissue mass overlying the right ilium that measured 9 cm. in diameter. X-ray films of the spine showed moderate scoliosis toward the right, which might have been due to splinting and muscle spasm. The kidney shadows were of average size and shape and in the usual position. There were no other areas of destruction in the pelvis, spine or the thoracic cage. Roentgenogram of the chest was negative.

Following admission, the patient seemed to be fairly comfortable so long as he was confined to bed. He continued to run a low-grade fever. Other white-cell counts were 13,900 and 19,200.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHANNING C. SIMMONS: There are some data that are not given in the protocol that might be of value in making a diagnosis. The blood chemical findings, for instance, would be of value in ruling out certain bone tumors, and a tuberculin test would help in ruling out tuberculosis of the sacroiliac joint. No mention is made of lymph-node involvement.

DR. BENJAMIN CASTLEMAN: The serum calcium was 9.4 mg. per 100 cc., the phosphorus 4.3 mg., and the phosphatase 1.7 Bodansky units. A tuberculin test was not done.

DR. SIMMONS: In other words the phosphatase was on the low side of normal. The serum protein would be of value in ruling out plasma-cell myeloma, which I doubt that this boy had.

Are the x-ray films available?

DR. LAURENCE L. ROBBINS: These films show a destructive process involving the ilium, with apparent extension up to but not involving the

one hour. Before we⁵ studied the fractional excretion of dye in nephritic patients, it was difficult to estimate prognosis on the basis of any single test. Our work showed that there were no survivals after one year if the dye excretion fell to 5 per cent or less in fifteen minutes, and it has proved on many occasions to have prognostic value. This case substantiates that.

DR. BUTLER: How about the weight? When they gave ammonium chloride, the serum protein increased. One wonders if that was an error on the part of the laboratory or whether the serum protein went up because of loss of edema and of weight.

DR. CHAPMAN: No weight is given on the first admission.

DR. BUTLER: If one is treating patients with cardiac failure and renal disease, an excellent way to tell what is going on is to weigh them now and then.

DR. CHAPMAN: My diagnoses are diabetes, arteriosclerosis, hypertension and intercapillary glomerulosclerosis — the type described by Kimmelstiel and Wilson. I believe that she died in kidney failure from that type of kidney disease and that she had an old pulmonary infarction at the left base. I do not believe that she had recent coronary occlusion with infarction of the anterior myocardial wall, but that these electrocardiographic changes were produced by pericarditis and effusion; possibly there was an old coronary occlusion that dated back to the first episode, two months before admission.

DR. WILLIAM BECKMAN: The patient had lost 20 pounds. On entry she weighed 139 pounds, and two weeks later 119.

DR. BUTLER: We can assume then that the ammonium chloride had a diuretic and a dehydrating effect, with the increase in serum protein that Dr. Chapman noted.

DR. BECKMAN: During the first admission she definitely improved clinically so far as decompensation was concerned. When I went over her the first time I thought of intercapillary glomerulosclerosis, but finally ruled it out because she did not have the retinopathy typical of diabetes. The retinal changes were characteristic of arteriosclerosis. So I decided that she had arteriosclerotic kidneys and hypertension.

DR. BUTLER: Can you tell us whether she really did have diabetes?

DR. BECKMAN: We were not certain, since we merely did the routine tests. She continued to excrete a little sugar each day. She never had a blood sugar higher than 155 mg. per 100 cc., and she was given insulin on the theory that all diabetic patients should receive insulin for three days.

DR. CHAPMAN: Was a glucose-tolerance test done? I am impressed by the number of patients in the Out Patient Department on whom a diagnosis of diabetes is made on a single test showing sugar in

the urine. It seems that glucose-tolerance tests are not done often enough to establish a definite diagnosis.

DR. BUTLER: In many of the patients you are speaking about there is no doubt about the diabetes. A typical history, a high blood sugar and sugar in the urine usually establish the diagnosis of diabetes. Thus there is no need of doing a glucose-tolerance test. In the doubtful case it is reasonable to ask for such a test.

DR. CHAPMAN: I agree.

CLINICAL DIAGNOSES

Chronic vascular nephritis, with uremia.
Hypertensive heart disease.
Congestive failure.

DR. CHAPMAN'S DIAGNOSES

Diabetes.
Arteriosclerosis.
Hypertension.
Intercapillary glomerulosclerosis.
Uremia.
Pericardial effusion.
Pulmonary infarction, left base?
Coronary occlusion (two months old)?

ANATOMICAL DIAGNOSES

Intercapillary glomerulosclerosis, marked.
(Uremia.)
Diabetes mellitus.
Myocardial infarction, recent and old.
Coronary sclerosis with old occlusion.
Cardiac hypertrophy, hypertensive type.
Hydrothorax, bilateral.
Bronchopneumonia, terminal.
Pericarditis, healing.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this patient showed a hypertrophied heart weighing 450 gm. The coronary arteries were markedly sclerotic, and in the descending branch of the left we found an old occlusion, with a corresponding healed infarct in the myocardium. In addition there were scattered through the left ventricular wall yellow and pinkish-red areas that looked like the lesions of acute infarction. Microscopic examination showed acute myocardial infarction, although we were unable to find a recent thrombosis. This infarction showed polymorphonuclear infiltration and necrosis of muscle fibers, so that I do not believe that there is any question about the diagnosis. Also, the involved areas were in the endocardial side of the myocardium rather than in the pericardial side, so that they were not due to an extension from the

icarditis, which at the time of autopsy was in the healing stage. There has been a lot of discussion about the appearance of the myocardium in patients with renal failure. Most people believe that there is no definite myocarditis due to renal failure. Though Gouley⁶ has stated that there is a characteristic myocardial degeneration.

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The patient had been well until three months before admission, when he slipped and fell on his right hip. He developed pain and limitation of

sacroiliac joint. The soft-tissue mass definitely extends into the pelvis.

DR. SIMMONS: What is the shadow at the hilus of the right lung?

DR. ROBBINS: It is possibly due to enlarged hilar nodes, but I could not be positive without fluoroscoping the patient.

DR. SIMMONS: The physical examination says that the abdomen was negative, and makes no men-

rather than in the body of the bone. I can rule out syphilis on account of the negative Hinton test.

I do not know of any systemic disease that gives an appearance of tumor, with bone destruction limited to one bone, associated with an elevated temperature and white-cell count.

Then there are the tumors. It might have been metastatic from either a tumor of the kidney or a neuroblastoma of the mediastinum or suprarenal



FIGURE 1. Roentgenogram of Pelvis.

tion of what, in the film, is obviously a shadow occupying the greater part of the pelvis.

In all cases of bone disease there are three groups of diseases to consider: first, an inflammatory condition, such as tuberculosis, osteomyelitis or syphilis; second, a systemic disease such as parathyroid or Paget's disease; and, third, some form of bone tumor, benign or malignant and either primary or secondary. I frankly cannot make a definite diagnosis on this boy, but on the basis of the facts given in the protocol and the x-ray findings I have to consider these three conditions.

Of the inflammatory conditions, because of the low-grade temperature, the history of trauma and the bone destruction, he might have had an osteomyelitis. I am not particularly concerned with tuberculosis, since it usually arises around the joint

gland. It might have been a primary bone tumor. An osteogenic sarcoma in this situation is unusual. A Ewing's sarcoma is quite common and often results in a somewhat elevated white-cell count and a low-grade fever. There is one other tumor that can simulate in bone practically every condition that I know, and that is a malignant lymphoma. A lymphoma can cause bone destruction and give a picture like that of osteomyelitis.

I frankly cannot make a diagnosis in this case. I believe that it was probably an osteomyelitis but cannot rule out a lymphoma or a Ewing's sarcoma. I should want a biopsy.

DR. ALLAN M. BUTLER: You would want a biopsy before considering therapy?

DR. SIMMONS: Very definitely. There is no use in giving therapy unless one knows what one is

ating. If it is malignant disease, one can give sufficiently heavy treatment; whereas if it is an inflammatory condition, this method of treatment should not be used. The radiologists are loath to treat any condition by x-ray unless a biopsy has established a diagnosis.

CLINICAL DIAGNOSIS

Osteomyelitis of ilium.

DR. SIMMONS'S DIAGNOSIS

Osteomyelitis of ilium?

Malignant lymphoma?

Ewing's sarcoma of ilium?

ANATOMICAL DIAGNOSIS

Ewing's sarcoma of ilium.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Apparently this mass must have been felt, as Dr. Simmons suggested, because they were able to puncture it with a needle and to aspirate a good-sized biopsy specimen. Microscopically the lesion proved to be a Ewing's sarcoma.

Preoperatively it was believed to be an osteomyelitis because of the sepsis, the high white-cell count and the fever. Following the biopsy the child was given a course of x-ray treatment and sent home. I recently heard from Dr. G. W. Van Gorder, who followed the patient, that within six weeks the child died of diffuse metastases to the lungs. I suppose that the shadow that Dr. Simmons pointed out in the chest film could have been a metastasis. Is that so, Dr. Robbins?

DR. ROBBINS: Probably.

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POSTWAR PLANNING

Of the approximately 55,000 medical officers now in military service, 3000 have been asked to express themselves concerning postwar medical training. Of these, 927 had replied up to June 1, and the answers to the questionnaire are reported in the June 24 issue of the *Journal of the American Medical Association*. If this sample is representative of the whole group, — and there is no reason to think that it is not, — a large order in postwar medical education is about to be placed.

Divided according to the dates of licensure, which are roughly parallel to the dates of graduation from the medical school and therefore to age groups, the 927 officers fell into the following groups: Group 1,

400 (43 per cent); Group 2, 323 (35 per cent); Group 3, 168 (18 per cent); and Group 4, 36 cent). Group 1 consisted of those licensed 1937 to 1943; Group 2, those licensed from 1936; Group 3, those licensed from 1920 to 1936; and Group 4, those licensed before 1920.

Of these Group 1 is the largest, and those trained in it are the youngest and the most in of postwar education. Many men in this group had their periods of medical training shortened hurried by the war, so that it is not surprising 90 per cent of them state that they will graduate between one and two years of additional training. If the ratio of 400:927 holds for the 55,000 officers the total number of Group 1 men — those who graduated subsequent to 1936 — will approximate 24,000.

Already about 300 of these 400 officers, or about 18,000 of the total, have stated that they wish to specialize, which means that residencies will be in demand. A previous survey has shown that there are in this country about 8000 residencies, and it was suggested that these facilities might be expanded to accommodate 12,000 in the immediate postwar period.* The necessity for a gradual demobilization is apparent if all the officers wishing training are to be accommodated without preliminary waiting periods, for there will be a greater load than the teaching hospitals of the country can possibly absorb in any one-year or two-year period. The replies of these young medical officers also indicate that rural communities will continue to find it difficult to attract doctors. Only 6 per cent expressed a preference for a rural location, the majority preferring a community of between 25,000 and 250,000 population.

To what extent this thinking on the part of the small sample analyzed represents the whole and to what extent the thinking of the whole may undergo future changes remain to be decided. For the present one can only visualize a postgraduate medical education program of unprecedented proportions — something that will have to bring into use a larger proportion of clinical material than has ever before been utilized.

*Medicine and the war: postwar graduate medical education. A preliminary report by the Council on Medical Education and Hospitals. *J. A. M. A.* 124:40, 1944.

Y IS A JAP?

THE magazine *Time*, although not ordinarily used as a journal of scientific reference, contains in its August 7 issue two items of more than ordinary interest regarding the Japanese behavior pattern. The first is an account by Robert Sherrod, *Time* correspondent, of the mass suicides on Saipan. The second is the news story of an analysis of Japanese character by Geoffrey Gorer, anthropological investigator in the Institute of Human Relations at Yale University.

The western world has become thoroughly accustomed to bizarre stories of the picturesque Japanese *seppuku* ceremony, considering the idea of it as something remote from our own usual mental processes. We know of how, in times of peace, the over-mind Japs were wont to toss themselves into the craters of hyperactive volcanoes; from our marines in the South Pacific and our soldiers on Iwate and Kiska we have more recently heard of the wholesale and apparently purposeless self-destruction practiced by the soldiers of the Emperor when faced with final defeat. This has frequently been not a matter of fighting to the last ditch. Soldiers have impaled themselves on the bayonets of the enemy or have fallen on their own swords or blown themselves to bits with hand grenades when they still had ammunition with which to continue fighting.

On Saipan, for the first time, our forces gained possession of territory with a considerable settled Japanese population, and so prevalent became suicide among the civilians of both sexes and all ages, according to Sherrod, that the question is raised whether the whole Japanese race will choose death to surrender.

Gorer, in his study of Japanese psychology, and with perhaps more than a slight leaning toward the Freudian concept, places great emphasis on the severe toilet training of the Japanese infant. Beginning at the age of four months the baby is held over the balcony or road at frequent intervals and for obvious reasons not at all suggestive of the Capulet and Montague affair. Lapses in conduct are punished with great severity. At six months he is

taught to bow respectfully (although the polite hissing through the teeth is waived), and before the end of the first year "he is forced to learn to sit stiffly on his haunches."

The male is taught that he belongs to the dominant sex, but even so his life is bound rigidly by convention. To overstep a rule of behavior brings ridicule without mercy from friend and foe, and so we find developed the repressions that have their outlet in cruelty and arrogance toward supposedly weaker individuals and races, and the dread of loss of face, which makes life intolerable in an environment that has become hostile.

We thus see in the rigid training of the Japanese both his strength and his weakness. It drives him on through hardship and danger with the endurance of a fanatic, but when it fails to achieve its goal he is finished. If we accept the thesis, however, that the modern Japanese is the product of an unfortunate environment and not a completely strange and different biologic mishap, then there is some hope of adapting future generations of the race to existence in a world that recognizes the rights of others.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BROWN — Edison W. Brown, M.D., of Revere, died August 18. He was in his sixty-ninth year.

Dr. Brown received his degree from Tufts College Medical School in 1905. He was a member of the American Medical Association and the New England Obstetrical Society and a staff member of the Chelsea Memorial Hospital, Whidden Memorial Hospital, Everett, and Winthrop Community Hospital.

His widow, his mother and two sisters survive.

COBB — Farrar Cobb, M.D., of Hyannis, died May 28. He was in his seventy-eighth year.

Dr. Cobb received his degree from Harvard Medical School in 1893. He served on the staff of the Massachusetts General Hospital and as superintendent of the Massachusetts Eye and Ear Infirmary. He was chief surgeon from 1930 to 1935 and on the consulting staff from 1930 to 1944 of the Cape Cod Hospital. He was a member of the American Medical Association and the New England Surgical Society and fellow of the American College of Surgeons.

DUNN — Lt. Raymond A. Dunn, of Worcester, was killed when the destroyer on which he was medical officer was sunk by enemy fire in the invasion of Sicily. He was in his thirty-fourth year.

Dr. Dunn received his degree from Tufts College Medical School in 1935. He was an obstetrician on the staff of St. Vincent Hospital. He was a member of the American Medical Association and the Worcester District Medical Society.

His parents, a sister and a niece survive.

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*Medicine and the war: postwar graduate medical education. A preliminary report by the Council on Medical Education and Hospitals. J. A. M. A. 124:40, 1944.

WHY IS A JAP?

THE magazine *Time*, although not ordinarily used as a journal of scientific reference, contains in its August 7 issue two items of more than ordinary interest regarding the Japanese behavior pattern. The first is an account by Robert Sherrod, *Time* correspondent, of the mass suicides on Saipan. The second is the news story of an analysis of Japanese character by Geoffrey Gorer, anthropological investigator in the Institute of Human Relations at Yale University.

The western world has become thoroughly accustomed to bizarre stories of the picturesque Japanese hara-kiri ceremony, considering the idea of it as something remote from our own usual mental processes. We know of how, in times of peace, the sober-minded Japs were wont to toss themselves into the craters of hyperactive volcanoes; from our marines in the South Pacific and our soldiers on Attu and Kiska we have more recently heard of the wholesale and apparently purposeless self-destruction practiced by the soldiers of the Emperor when faced with final defeat. This has frequently been not a matter of fighting to the last ditch. Soldiers have impaled themselves on the bayonets of the enemy or have fallen on their own swords or blown themselves to bits with hand grenades when they still had ammunition with which to continue fighting.

On Saipan, for the first time, our forces gained possession of territory with a considerable settled Japanese population, and so prevalent became suicide among the civilians of both sexes and all ages, according to Sherrod, that the question is raised whether the whole Japanese race will choose death to surrender.

Gorer, in his study of Japanese psychology, and with perhaps more than a slight leaning toward the Freudian concept, places great emphasis on the severe toilet training of the Japanese infant. Beginning at the age of four months the baby is held over the balcony or road at frequent intervals and for obvious reasons not at all suggestive of the Capulet and Montague affair. Lapses in conduct are punished with great severity. At six months he is

taught to bow respectfully (although the polite hissing through the teeth is waived), and before the end of the first year "he is forced to learn to sit stiffly on his haunches."

The male is taught that he belongs to the dominant sex, but even so his life is bound rigidly by convention. To overstep a rule of behavior brings ridicule without mercy from friend and foe, and so we find developed the repressions that have their outlet in cruelty and arrogance toward supposedly weaker individuals and races, and the dread of loss of face, which makes life intolerable in an environment that has become hostile.

We thus see in the rigid training of the Japanese both his strength and his weakness. It drives him on through hardship and danger with the endurance of a fanatic, but when it fails to achieve its goal he is finished. If we accept the thesis, however, that the modern Japanese is the product of an unfortunate environment and not a completely strange and different biologic mishap, then there is some hope of adapting future generations of the race to existence in a world that recognizes the rights of others.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BROWN — Edison W. Brown, M.D., of Revere, died August 18. He was in his sixty-ninth year.

Dr. Brown received his degree from Tufts College Medical School in 1905. He was a member of the American Medical Association and the New England Obstetrical Society and a staff member of the Chelsea Memorial Hospital, Whidden Memorial Hospital, Everett, and Winthrop Community Hospital.

His widow, his mother and two sisters survive.

COBB — Farrar Cobb, M.D., of Hyannis, died May 28. He was in his seventy-eighth year.

Dr. Cobb received his degree from Harvard Medical School in 1893. He served on the staff of the Massachusetts General Hospital and as superintendent of the Massachusetts Eye and Ear Infirmary. He was chief surgeon from 1930 to 1935 and on the consulting staff from 1930 to 1944 of the Cape Cod Hospital. He was a member of the American Medical Association and the New England Surgical Society and fellow of the American College of Surgeons.

DUNN — Lt. Raymond A. Dunn, of Worcester, was killed when the destroyer on which he was medical officer was sunk by enemy fire in the invasion of Sicily. He was in his thirty-fourth year.

Dr. Dunn received his degree from Tufts College Medical School in 1935. He was an obstetrician on the staff of St. Vincent Hospital. He was a member of the American Medical Association and the Worcester District Medical Society.

His parents, a sister and a niece survive.

BREED — William B. Breed, M.D., of Newton, died August 21. He was in his fifty-second year.

Dr. Breed received his degree from Harvard Medical School in 1920. At the time of his death he was a member of the Committee on Publications and a counselor of the Massachusetts Medical Society, and chairman of its War Participation Committee. He was associate editor of the *Journal* from 1923 to 1937, and a member of the editorial staff from 1937 to 1942. He was a staff member at the Massachusetts General Hospital and an associate in medicine at Harvard Medical School. He was also a member of the American Medical Association, the American College of Physicians, the New England Heart Association and the American Clinical and Climatological Society.

His widow and three children survive.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

SARGENT — Frank H. Sargent, M.D., of Pittsfield, New Hampshire, died July 11. He was in his eighty-third year.

Dr. Sargent received his degree from Dartmouth Medical School in 1889. He was a member of the American Medical Association, the New Hampshire Medical Society, and the Merrimack County Medical Society.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN

CLINIC	DATE.	CLINIC CONSULTANT
Haverhill	September 6	William T. Green
Lowell	September 8*	Albert H. Brewster
Salem	September 11*	Paul W. Hugenberger
Brockton	September 14	George W. Van Gorder
Worcester	September 15	John W. O'Meara
Pittsfield	September 18	Frank A. Slowick
Springfield	September 20	Garry deN. Hough, Jr.
Fall River	September 25	Eugene A. McCarthy
Hyannis	September 26	Paul L. Norton

*Date changed.

CORRESPONDENCE

ANTERIOR POLIOMYELITIS

To the Editor: I have been much interested lately in reading in *Life* the account of the work being done by medical men in North Carolina during the existing epidemic of infantile paralysis.

The statement therein to the effect that these doctors are examining flies in the search for probable means of transmission brings back to my mind very distinctly my experience with that disease in this city some thirty years ago. At that particular time, since I was chairman of the Board of Health, and in contact with the official representative of the State Board of Health, as well as an epidemiologist, I was in a position to see most of the cases of that disease — not only my own patients, but many others; and I was much impressed at the time in observing on the bodies of many of the victims small discolored, concrete areas, which clearly had the appearance of being insect bites.

In my report to the State Board of Health I called attention to this fact. Nothing came of it, however; but I believed at the time, and have believed ever since, that there was to be sought the possible cause of the invasion.

Furthermore, it appeared that shortly before the first cases were reported, — which happened to be my own, — there

were three cases in one locality where a number of pigs in the vicinity all died within a short time; and it was that, before they died, each one was a victim of paralysis. In my opinion this was due to some insect with a very limited radius of activity, as the disease was not general, but confined to certain territories, where the afflicted persons adjacent to one another.

I hope this study in North Carolina will bring forth something worth while.

WILLIAM H. KELEHER, M.D.

48 Pleasant Street
Woburn, Massachusetts

NOTICES

ANNOUNCEMENT

Dr. Alice Nauen announces the removal of her office from 121 Sutherland Road, Brookline, to 41 Concord Avenue, Cambridge 38.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, September 7, in the classroom of the Nurses' Residence at 7:15 p.m. Dr. Louis K. Diamond will speak on the subject "The Rh Factor." Dr. Hildur Gibs will be chairman.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 7

THURSDAY, SEPTEMBER 7

7:15 p.m. The Rh Factor. Dr. Louis K. Diamond. New England Hospital for Women and Children.

SATURDAY, SEPTEMBER 9

*10.00-11.30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, SEPTEMBER 11

International Association of Industrial Accident Boards. Hotel Statler, Boston.

*12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, SEPTEMBER 12

International Association of Industrial Accident Boards. Hotel Statler, Boston.

*12:15-1:15 p.m. Clinicorontgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, SEPTEMBER 13

International Association of Industrial Accident Boards. Hotel Statler, Boston.

*12.00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 6-9. American Congress of Physical Therapy. Page 248, issue of August 10.

OCTOBER 2-7. Seminar in Legal Medicine, Harvard Medical School. Page 110, issue of July 20.

OCTOBER 3-5. American Public Health Association. Page ix, issue of March 30.

OCTOBER 4. Medicolegal conference, Mallory Institute of Pathology, Boston. Page 110, issue of July 20.

OCTOBER 9-20. 1944 Graduate Fortnight of the New York Academy of Medicine. Page xvii, issue of July 27.

OCTOBER 16-NOVEMBER 3. Third Postgraduate Course in Industrial Medicine.

OCTOBER 30. New York Institute of Clinical Oral Pathology, New York Academy of Medicine. Page 110, issue of July 20.

NOVEMBER 2-4. Association of Military Surgeons. Page xliii, issue of August 17.

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PAGET'S DISEASE: ITS PATHOLOGIC PHYSIOLOGY AND THE IMPORTANCE OF THIS IN THE COMPLICATIONS ARISING FROM FRACTURE AND IMMOBILIZATION*

EDWARD C. REIFENSTEIN, JR., M.D.,† AND FULLER ALBRIGHT, M.D.‡

BOSTON

THE purpose of this paper is to call attention to the occurrence of acute atrophy of bone (osteoporosis) as a complication of Paget's disease, and to discuss the seriousness and implications of this situation as illustrated by two case histories. In order to make the subsequent presentation clear, it will be necessary first to discuss briefly normal bone metabolism, the metabolic abnormalities in osteoporosis as opposed to those in osteomalacia and osteitis fibrosa generalisata, the morbid anatomy of Paget's disease and finally a concept concerning the pathologic physiology in Paget's disease. It is regretted that some repetition of previous presentations¹⁻⁴ is unavoidable.

NORMAL BONE METABOLISM

Normal bone is composed of an organic matrix in which is deposited a calcium-phosphate-carbonate salt. It has three types of surface — one on which nothing is happening, one on which bone is being resorbed and one on which bone is being formed (Fig. 1). Where bone is being resorbed, one sees osteoclasts. Bone formation consists of two steps — the laying down of the matrix by osteoblasts and the deposition therein of the calcium salt.

It should be emphasized that bone formation and bone resorption occur at one and the same time. The reason why the body can deposit calcium on one surface while it is being resorbed on another is probably connected with the enzyme phosphatase. It is thought that the enzyme is made by the osteoblasts and that its presence where bone matrix is being formed increases the local concentration of phosphate ions by the splitting off of these ions from organic phosphate compounds, and hence promulgates the deposition of a calcium-phosphate-carbonate salt. In the absence of hepatic disease,

the serum alkaline phosphatase level is an index of the activity of the osteoblasts. In the presence of excessive osteoblastic activity the serum phosphatase level rises; with osteoblastic inactivity it tends to fall. Since the normal level of the serum phosphatase is extremely low, however, this fall is not usually discernible.

There is considerable evidence that stresses and strains strongly stimulate the osteoblasts to lay down bone matrix: the greater the stresses and strains, the greater is the bone formation. Thus, persons whose occupations involve considerable physical activity have heavy skeletons, whereas those with sedentary occupations tend to have light bones.

OSTEOPOROSIS, OSTEOMALACIA AND OSTEITIS FIBROSA GENERALISATA

Osteoporosis, osteomalacia and osteitis fibrosa generalisata have one thing in common, a decreased bone mass. The total bone mass may be diminished to a pathologic degree from either an increase in bone resorption or a decrease in bone formation. The former is called "osteitis fibrosa generalisata" (Fig. 1) and is found in hyperparathyroidism. As will be seen later, it has certain points in common with Paget's disease. A decrease in bone formation may result either from an underactivity of the osteoblasts in laying down bone matrix or from a failure in the deposition of calcium salts in this matrix: the former is termed "osteoporosis," and the latter "osteomalacia" (Fig. 1).

Since the cases to be reported represent, in the final analysis, the imposition of osteoporosis on Paget's disease, it is desirable to discuss this condition in more detail. The causes of osteoporosis include old age, lack of stresses and strains to stimulate the osteoblasts, — for example, immobilization,³ — lack of estrin to stimulate the osteoblasts — for example, postmenopausal osteoporosis^{1,2} — and lack of protein to provide material for the matrix, such as is found, according to our conception, in

*From the Department of Medicine, Harvard Medical School, and the Medical Service of the Massachusetts General Hospital.

The expenses of this investigation were defrayed in part by a grant from the Josiah Macy, Jr., Foundation of New York.

†Research fellow in medicine, Harvard Medical School, graduate assistant in medicine, Massachusetts General Hospital.

‡Associate professor of medicine, Harvard Medical School, physician, Massachusetts General Hospital.

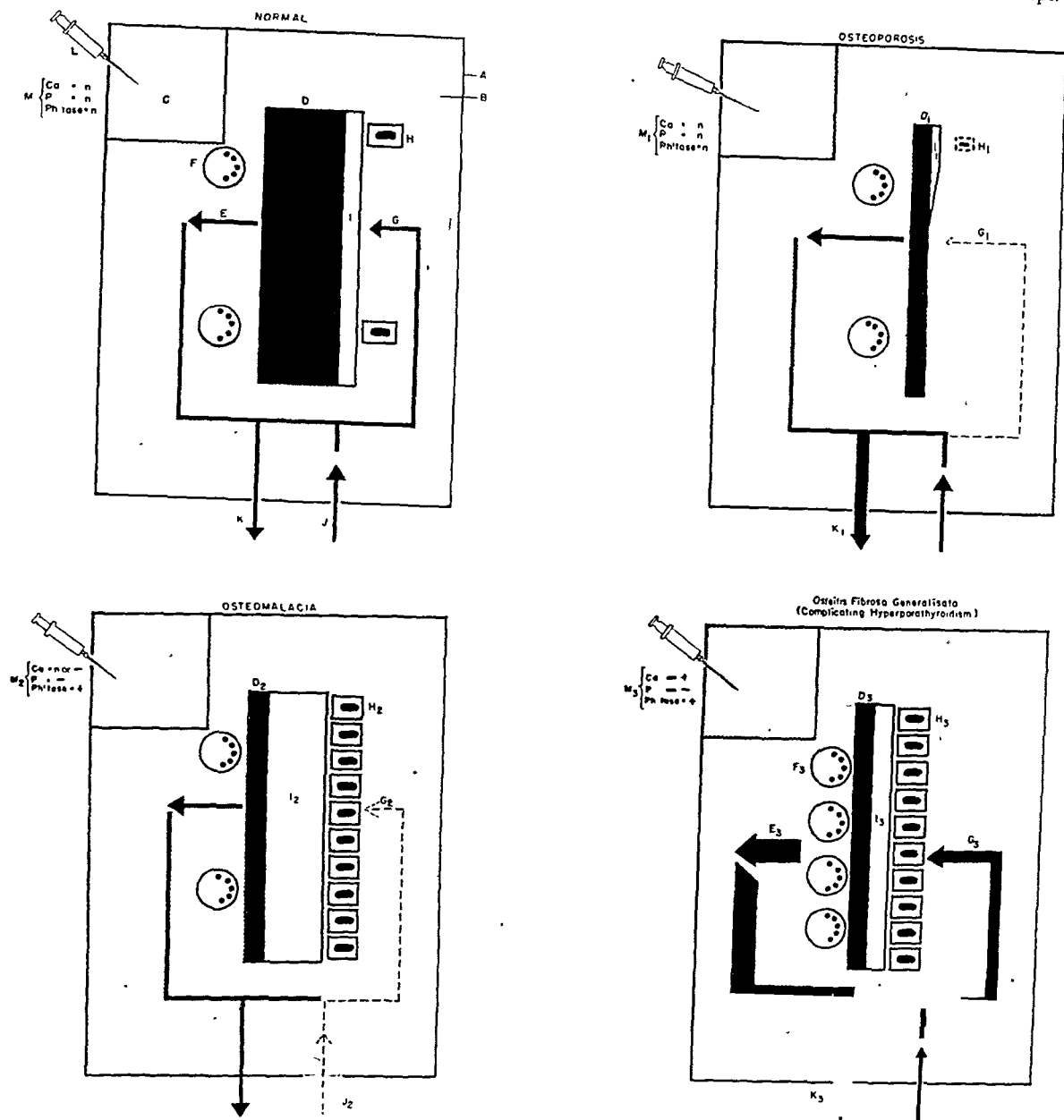


FIGURE 1. Schematic Diagrams Showing the Differences in Bone Metabolism between Normal, Osteoporosis, Osteomalacia and Osteitis Fibrosa Generalisata Complicating Hyperparathyroidism (reproduced by permission of the Journal of the American Medical Association).

In all the diagrams, the designations are as follows: A — body limits; B — body fluid, C — body serum, a compartment of body fluid easy to tap for analysis; D — bone mass with two surfaces, one where bone is being resorbed and one where it is being laid down; E — arrow indicating by its size the rate of calcium and phosphorus resorption; F — osteoclast; G — rate of calcium and phosphorus deposition; H — osteoblast laying down osteoid (I); J — calcium and phosphorus entering the gastrointestinal tract; K — calcium and phosphorus leaving the body by the kidneys and other exits; L — syringe for obtaining serum for analysis; M — blood values (N, normal; +, high; and —, low).

NORMAL. Note that the deposition of calcium and phosphorus (G) equals the resorption (E) and that part of the latter goes back into the bone.

OSTEOPOROSIS. Note the decrease in bone mass (D₁), the primary hyperplasia of osteoblasts (H₁), the decreased deposition of osteoid (I₁), the decreased deposition of calcium and phosphorus (G₁), the increased excretion of calcium and phosphorus (K₁) and the normal blood values (M₁).

OSTEOMALACIA. Note the decrease in bone mass (D₂), the hyperplasia of osteoblasts (H₂) because of increased stresses and strains, the increased deposition of osteoid (I₂) inadequately calcified because of the low serum calcium and phosphorus values, the decreased deposition of calcium and phosphorus (G₂), the primary difficulty in absorbing calcium and phosphorus from the gastrointestinal tract (J₂) and the abnormal blood values (M₂).

OSTEITIS FIBROSA GENERALISATA COMPLICATING HYPERPARATHYROIDISM. Note the increased excretion of calcium and phosphorus in the urine (K₃), the increased resorption of calcium and phosphorus (E₃), the increase of osteoclasts (F₃), the decreased bone mass (D₃), the increased bone formation by osteoblasts (I₃) because of increased stresses and strains, the increased deposition of calcium and phosphorus (G₃) because the serum is not undersaturated in respect to calcium phosphate, and the high phosphatase level (M₃).

Cushing's syndrome,^{4,5} in the osteopathies of starvation and probably in the demineralization associated with hyperthyroidism.

Osteoporosis being by definition primarily a disorder of tissue metabolism and only secondarily one of calcium metabolism, no alteration in the serum calcium and phosphorus levels is to be expected, nor is one usually found. Since in osteoporosis bone formation decreases and bone resorption continues unabated, however, hypercalciuria occurs, and may lead to the same kidney complications as are found in hyperparathyroidism, in which the hypercalciuria results from the hypercalcemia.

The degree of hypercalciuria — the diet being constant — depends on the discrepancy between bone destruction and bone formation. If osteoporosis develops gradually, this discrepancy is at no time great and hypercalciuria is not marked. If, on the other hand, bone formation suddenly stops in a nonosteoporotic skeleton, there is marked hypercalciuria — for example, artificial menopause or immobilization of the skeleton in a cast. Furthermore, in young subjects, in whom the turnover of bone is more prominent than in older ones, a sudden curtailment of bone formation results in a marked imbalance.

There was recently reported from this laboratory³ the case history of an active fourteen-year-old boy who fractured his leg and had a large part of his skeleton immobilized by a cast. So great was the resulting decrease in bone formation that not only hypercalciuria but also hypercalcemia occurred. The cause of the latter was an inability of the kidney to excrete the calcium as rapidly as it came from the skeleton. Since the hypercalcemia suggested hyperparathyroidism, the patient was subjected to two operations in an effort to find a parathyroid tumor before the true situation became apparent. The hypercalcemia soon disappeared when he was mobilized. The cases reported below illustrate another situation in which a serious state from acute atrophy of disuse (osteoporosis) occurred.

MORBID ANATOMY OF PAGET'S DISEASE

If one defines a "localized bone disease" as any disease that is not generalized, Paget's disease is localized. It may be limited to one bone or be widely spread throughout many bones, but it is not generalized. One can almost invariably find somewhere a sharp line of demarcation between normal bone on one side and Paget's disease on the other. The very fact that Paget's disease is not generalized is strong evidence against its being a metabolic or endocrinologic disorder. The reader may well ask, "What about the bone cysts in hyperparathyroidism?" But these are secondary complications; the underlying lesion, decalcification, is generalized. The reader may then ask, "What about postmenopausal osteoporosis, in which the bone

lesions tend to be confined to the spine and pelvis?" Here the disease is following a well-defined pattern; certain parts of the skeleton are more prone to involvement than others and the distribution of the lesions is not spotty but according to plan; it is not as though the twelfth thoracic and third

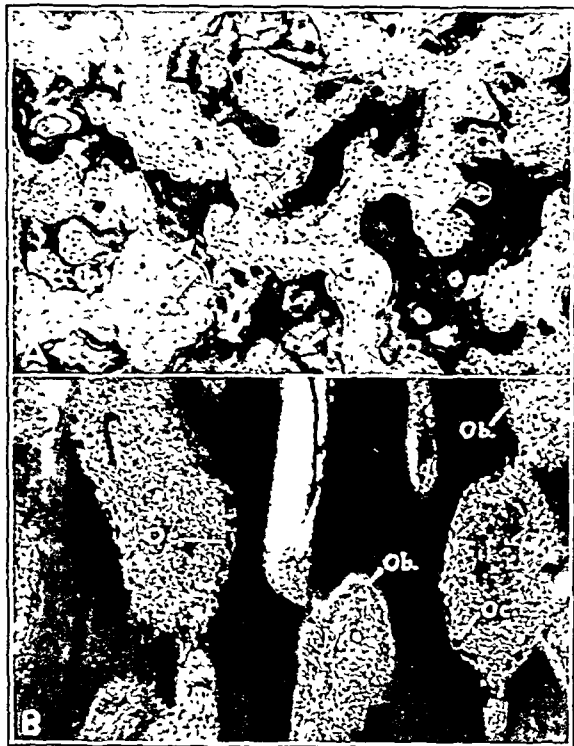


FIGURE 2. Photomicrographs of the Bone in Paget's Disease (A) and Hyperparathyroidism (B).

Note that although the osteoclasts (Oc.) and the osteoblasts (Ob.) are present in both diseases the structural integrity has disappeared in A but is maintained in B. Note also the mosaic appearance of the cement lines, some of which are indicated by arrows. (These photographs were kindly supplied by Dr. Granville A. Bennett, to whom the authors are greatly indebted.)

lumbar vertebrae were involved whereas the remaining vertebrae were normal.

Having made the above rather dogmatic statement, we must make one reservation. We have in our clinic a patient with undoubted Paget's disease in whom every bone in the body is involved; moreover, each bone is at the same stage of the disease. Unfortunately, the patient refuses to be hospitalized for detailed studies.

When one comes to the actual bone lesion in Paget's disease, it has much in common with that seen in osteitis fibrosa generalisata (compare Fig. 2A and B). In both conditions the bone lesions are extremely vascular, there is marked fibrosis, about half the bone surface is covered with osteoclasts as evidence of marked bone resorption and about half with osteoblasts as evidence of marked bone repair, and the bone that is being laid down

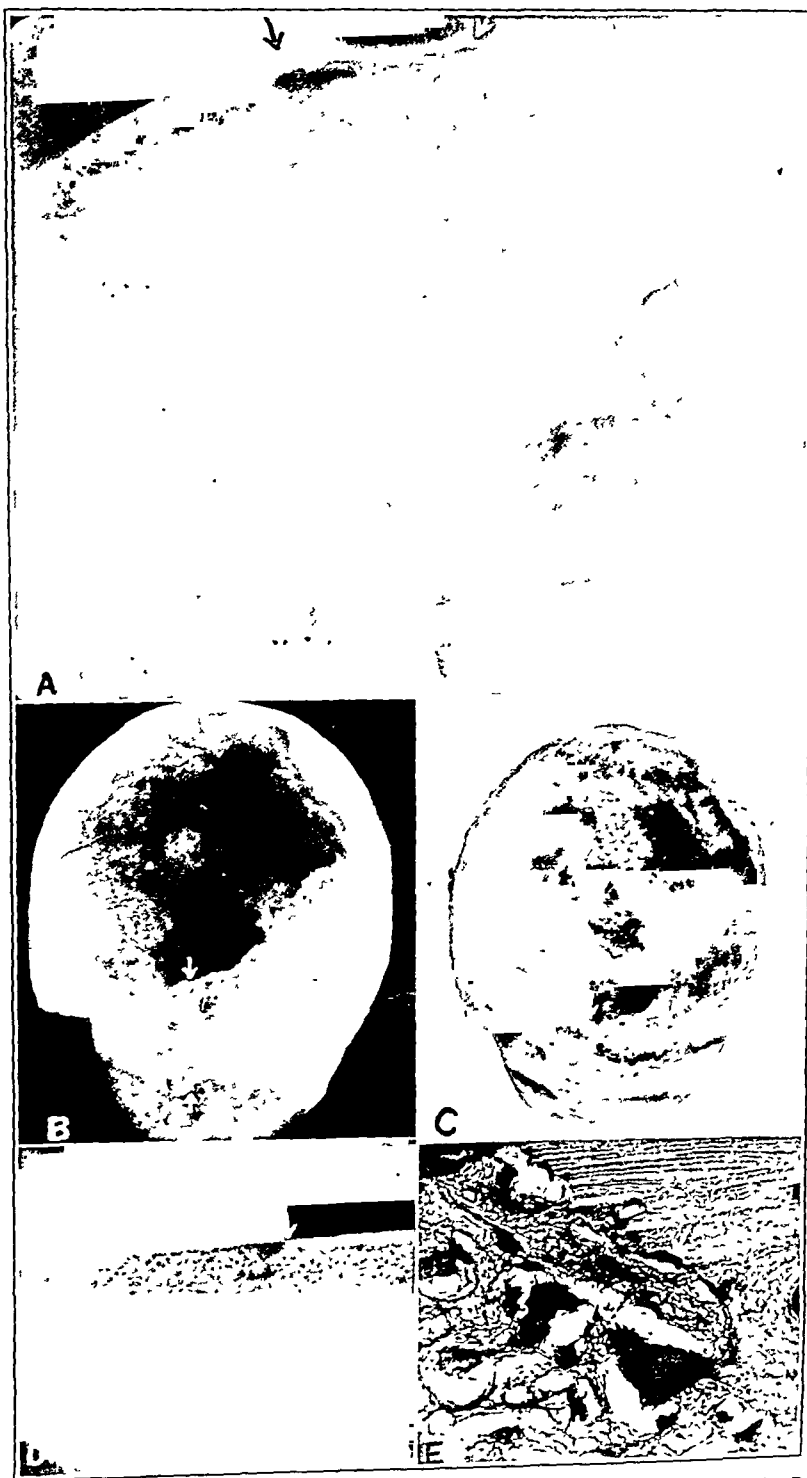


FIGURE 3 Photographs Showing That the Initial Lesion in Paget's Disease is Bone Destruction.

A — the x-ray film of a skull with two areas of destruction separated by a bridge of normal bone (between the arrows). B — the x-ray film of the same skull post mortem. C — the skull as it appeared post mortem. D — a section through this skull showing the advancing edge of destruction (arrow), with normal bone to the right and involved bone to the left. E — a photomicrograph of the area at the point of the arrow in D, showing normal bone on the right and the initial lesion of bone destruction on the left with osteoclasts (arrow) in juxtaposition to the normal bone.

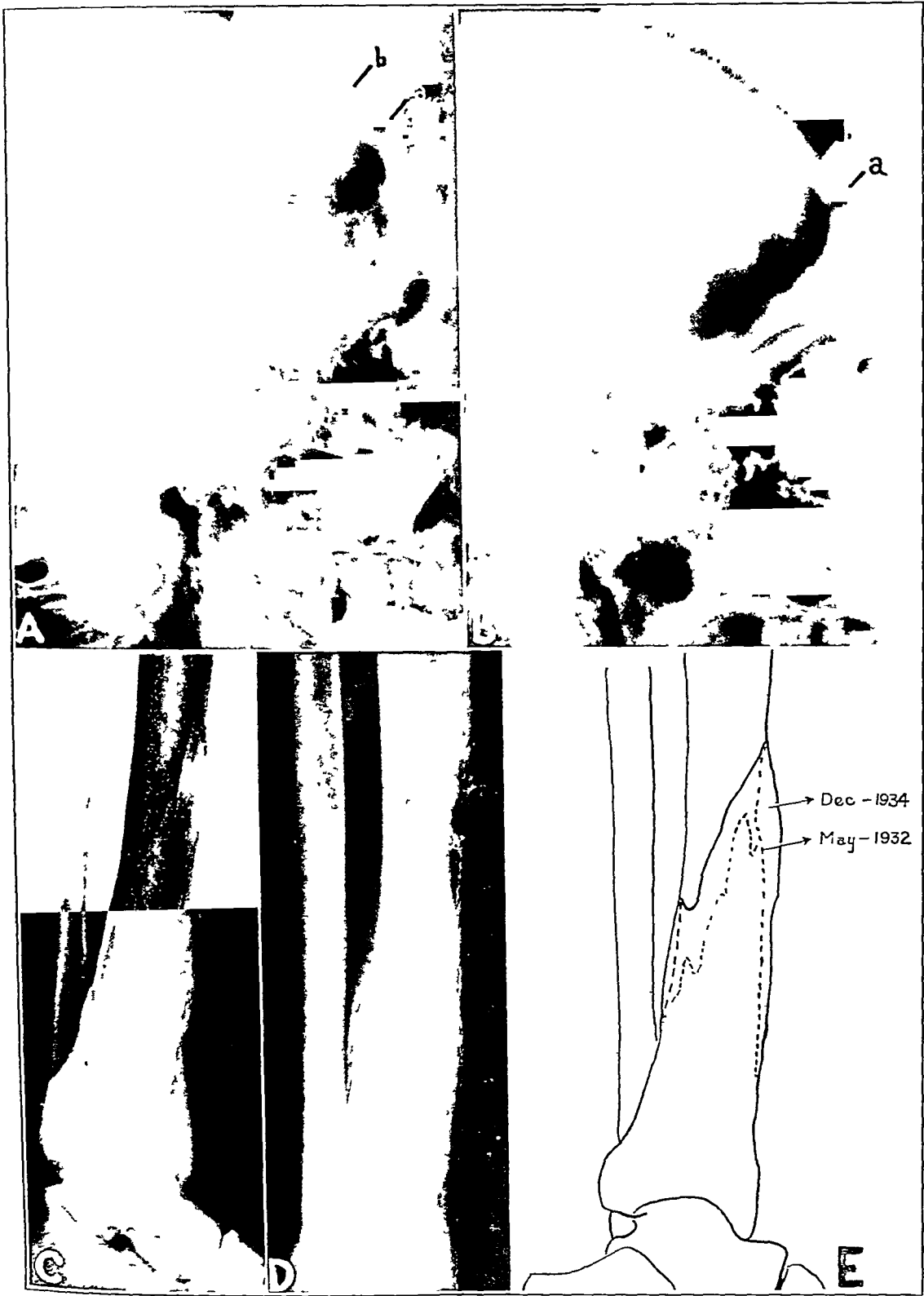


FIGURE 4 The Progression of Paget's Disease

A — skull showing an area of destruction (a to b) and normal bone to the right and overgrown bone to the left. B — the same skull two years later showing that the area of destruction has moved closer to the nose. C — involvement of the tibia. D — same tibia two and a half years later. E — diagram indicating the progression of the lesion in the tibia.

is being calcified, as shown by the normal width of the osteoid seams. There are, however, some differences. There is not the same tendency to the formation of so-called "osteoclastomas" or brown tumors in Paget's disease as in osteitis fibrosa generalisata. The most important distinction between the two conditions, however, concerns the architecture of the bone. In Paget's disease, for reasons that will appear below, the trabeculae start nowhere and end nowhere; in osteitis fibrosa generalisata there may be extreme decalcification, but those trabeculae that are left are in good mechan-

what is going on in a complicated pathologic picture, one should always try to get at the advancing edge of the lesion and see what comes first.

In the skull in Paget's disease one often finds lesions that have quite a different appearance from those encountered in other parts of the skeleton. They lack the marked overgrowth of bone and consist merely of circumscribed areas of bone destruction. The x-ray appearance of such a lesion is shown in Figure 3A. The involved area terminates abruptly (see arrows). At autopsy, a section through such an area (Fig. 3D) showed normal



FIGURE 5. X-ray Films of Paget's Disease (Case 1), Showing the Right Femur Immediately (A), Fourteen Weeks (B) and Seven Months (C) after the Fracture. Compare the densities of the cortex at the points indicated by the arrows.

ical arrangement. A third difference between the two conditions has to do with the so-called "mosaic structure," as first described by Schmorl.⁶ This pathognomonic feature of Paget's disease is due to the bizarre arrangement of the cement lines within the trabeculae (see arrows in Fig. 2). To be sure, there are other bone diseases with an increased number of cement lines in the trabeculae, but the lines are not so completely irregular. The reason for them will be discussed below.

From the above discussion, it is evident that in Paget's disease there is a marked increase in both bone destruction and bone formation; in other words, there is an increased turnover of bone. If one had to guess, one would presumably suppose that the increased bone formation was the result of increased bone destruction. But one does not have to guess; one can examine the initial lesion. To discover

bone (to the right of the arrow) sharply demarcated from the involved bone (to the left of the arrow). A microscopic examination at this point (Fig. 3E) revealed normal bone (to the right) being destroyed by the destructive lesion (to the left), with numerous osteoclasts; no bone formation or osteoblasts were seen. This is strong evidence that the initial lesion in Paget's disease is bone destruction.

Support for this contention can be derived from the characteristic manner in which the disease progresses. Thus, x-ray films of an involved skull (Fig. 4A) show three zones: normal bone (to the right of a), bone destruction (a to b) and bone repair with overgrowth and increased density (to the left of b). If such an area of involvement is followed for several years, the zone of bone destruction in some cases may be seen to advance. Such was the case in this skull, in which the lesion advanced into

the normal bone closer to the nose (Fig. 4B). In the long bones, for reasons that will appear below, the bone repair usually occurs almost simultaneously with the bone destruction, and one seldom has the opportunity to see one process divorced from the other; occasionally, where one does (Fig. 4C, D and E) the same sequence of zones appears. Schmorl⁶ demonstrated that the initial lesion in the long

of albumin. The sediment contained no casts, a rare red cell and 15 white cells per high-power field.

The leg was placed in traction, with a Kirschner wire through the lower end of the femur and a Hodgson splint with a Pierson attachment. The patient was allowed to take as much milk as he desired. He remained comfortable for 2 weeks, but then he began to complain of anorexia, headache and peculiar sensations of dryness in the back of the throat, associated with difficulty in swallowing. The patient attributed these symptoms to his "chronic sinusitis"; an otolaryngologist considered this probable, although he

TABLE 1. Chemical Determinations in Case 1.

DATE	BLOOD SERUM LEVELS				URINE		REMARKS
	CALCIUM	PHOSPHORUS	PHOSPHATASE	NONPROTEIN NITROGEN	CALCIUM QUASI-QUANTITATIVE TEST*	SPECIFIC GRAVITY	
	mg./100 cc.	mg./100 cc.	Bodansky units	mg./100 cc.			
8/14/41	—	—	—	—	—	1.028	Fracture; leg immobilized; milk ad lib.
8/30/41	—	—	—	—	—	1.008	Headache, anorexia, possible sinusitis and dysphagia
9/10/41	13.4	4.2	4.3	56	—	1.010	Epigastric distress, nausea and vomiting
9/26/41	13.2	4.1	—	68	+++	1.008†	Epigastric distress, nausea and vomiting
10/17/41	12.2	4.0	—	36	—	1.016	Patient somewhat better
10/30/41	—	—	—	—	—	—	Milk stopped; water forced.
11/ 5/41	10.5	5.6	6.1	—	+	—	Patient much better
11/15/41	—	—	—	—	—	1.017†	No complaints

*Sulkowitch test.

†Urine-concentration test.

bones is also bone resorption. He did this by making a longitudinal section of an involved long bone, from which he took a cross section 2 cm. distal to the point where the bone was involved grossly enough to be detectable by the naked eye. This cross section showed bone destruction without any evidence of bone formation.

CASE REPORTS

CASE 1* (M. G. H. 316138). The patient, a 58-year-old salesman, was admitted to the Phillips House on August 14, 1941. At the age of 22 he was aware of bowing of the left tibia. At the age of 28 he stepped into a hole and fractured the left tibia. X-ray examination revealed Paget's disease in the area of the fracture. This break healed without incident. At the age of 52 he fell down a flight of stairs and fractured the neck of the right femur. X-ray examination showed that this break also had been through an area of Paget's disease. The bones healed poorly, and finally a plate was inserted. Eight months after the fall, the patient was allowed to get about on crutches. He again fell and fractured the right femur in nearly the same place. He was placed in traction for 7 weeks and then in a plaster cast for 8 weeks. Eventually he was able to walk without crutches. On the day of admission, he was involved in an automobile accident, and for the third time fractured the neck of the right femur (Fig. 5A).

The past history revealed several interesting points. For many years the patient had consumed a large amount of milk—between 5 and 5 glasses a day. In his travels as a salesman, he had been in the habit of stopping for a milkshake several times a day, and in addition he had drunk milk at each meal. Also from time to time he had taken excessive amounts of alkalis for gastric distress. For more than 20 years he had been troubled with so-called "chronic sinusitis," with postnasal discharge and pain in the cheekbones.

Urinalysis shortly after admission showed a clear specimen with a pH of 5.0, a specific gravity of 1.028 and a slight trace

could find little on examination, and advised spraying the throat. The patient obtained no relief from this, but began to have epigastric distress, nausea and occasional vomiting. Urine examination at this time showed a specific gravity of

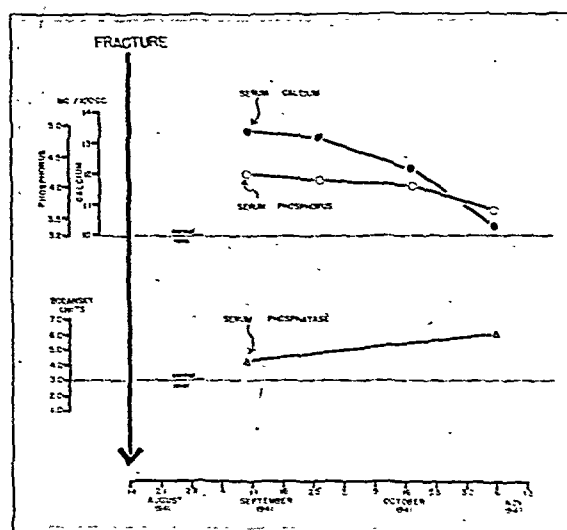


FIGURE 6. Chart Illustrating the Effect of Fracture on the Serum Calcium, Phosphorus and Phosphatase Levels in Paget's Disease (Case 1).

1.01, no albumin, a rare red cell and 2 white cells per high-power field. The serum nonprotein nitrogen was 56 mg. per 100 cc.

On September 10, 1941, approximately 4 weeks after the fracture, the serum calcium was 13.4 mg. per 100 cc., the serum phosphorus 4.2 mg., and the serum phosphatase 4.3 Bodansky units. These studies were repeated 2 weeks later with essentially similar findings (Fig. 6 and Table 1). At that

*This patient was seen through the courtesy of Dr. O. S. Staples and Dr. T. A. Warthin.

time the nonprotein nitrogen was 68 mg per 100 cc. A urine concentration test showed that the specific gravity was fixed at 1.008, but a phenolsulfonephthalein test showed 20 per cent of the dye excreted in 15 minutes. During the next 3 weeks

was permanently stopped and the intake of other fluids was increased. Within 1 week the patient was feeling much better. The serum calcium was 10.3 mg per 100 cc, the phosphorus 3.6 mg, and the phosphatase 6.1 Bodansky units.

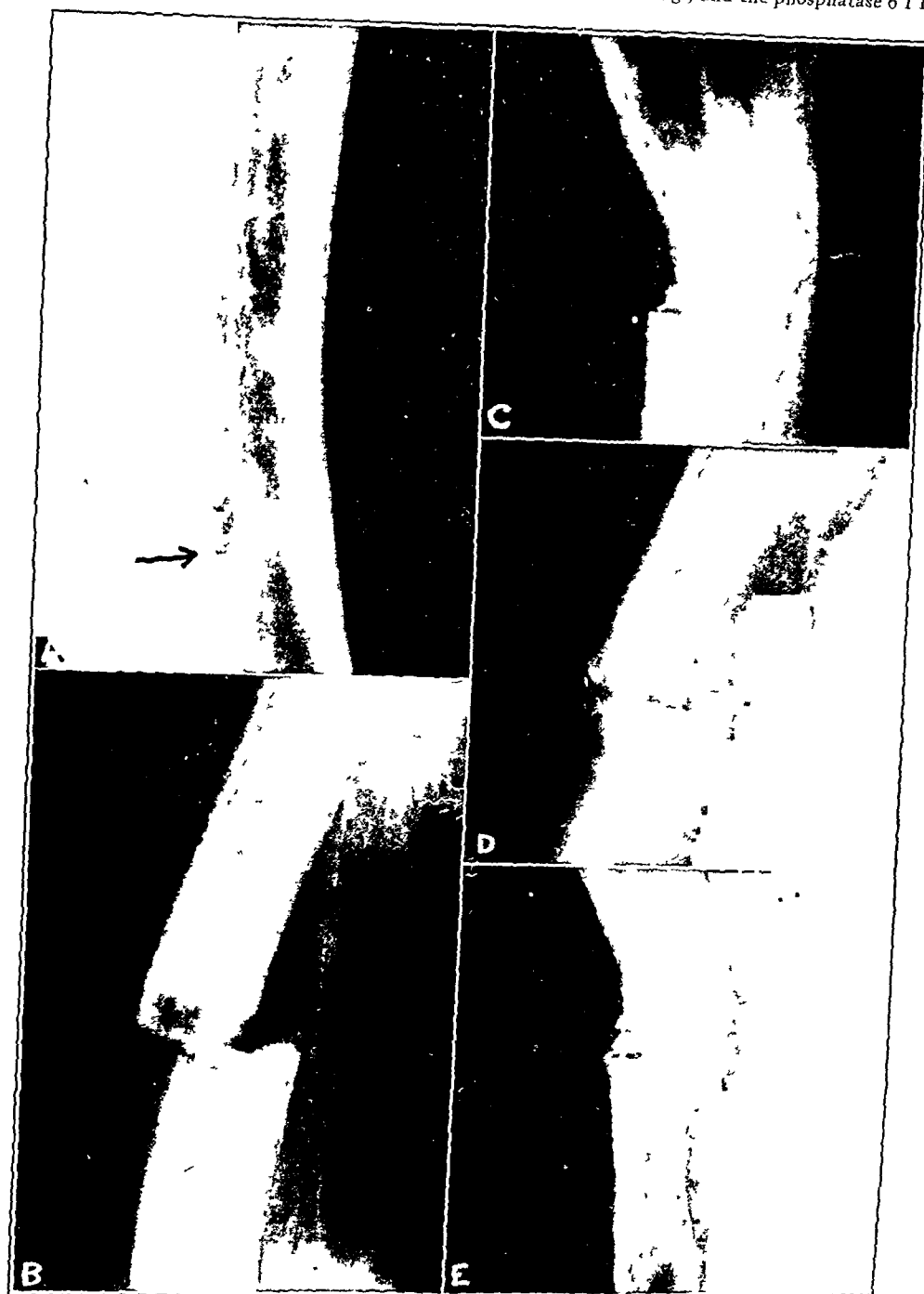


FIGURE 7 X-ray Films of Paget's Disease (Case 2), Showing the Right Femur three years before (A) immediately (B), three weeks (C), five weeks (D) and ten weeks (E) after fracture. The point of fracture is indicated by the arrow. Compare the densities of the cortex in these films.

the patient continued to have gastric distress. The water intake was increased and milk was omitted from the diet for several days, the serum findings were as follows: calcium, 12.2 mg per 100 cc, phosphorus, 4.0 mg, protein, 6.4 gm, and nonprotein nitrogen, 36 mg.

On October 30, because of our concept regarding the pathologic physiology of Paget's disease (see below), the milk

He was able to concentrate his urine to a specific gravity of 1.017. Thereafter he had an uneventful convalescence, except that the fracture healed very slowly. He was discharged July 11, 1942, 11 months after admission.

CASE 2 (M G H 281615) The patient, a 64-year-old woman, was admitted to the hospital on December 28, 1942,

with a fractured femur. At the age of 50 she became aware of enlargement of the head and the left clavicle. X-ray examination revealed Paget's disease. At the age of 57 she noticed bowing of the femurs. For some years she had been troubled with increasing deafness and ringing in the ears. She had never passed gravel. A physiologic menopause without hot flashes had occurred at the age of 52. In June, 1939, she was referred to one of us (F.A.) by Dr. Louis Hamman, of Baltimore.

The x-ray films of the femurs obtained in 1939 (Fig. 7A) had been used for teaching purposes to explain why it is possible in Paget's disease for a bowed leg to be as long as, if



FIGURE 8. *Paget's Disease Showing Fracture through the Site of a Previous Infraction.*

Other infractions above and below the fracture are indicated by arrows

not longer than, the unbowed leg. (The question was raised and answered by Schmorl.⁶) It will be seen that a series of partial fractures occurred on the convex side that led to an increase in length of a fraction of a centimeter for each fracture. It can be appreciated that it would not be difficult to produce a complete fracture at one of these points. The site at which the fracture subsequently developed is indicated by the arrow. (That this is not an isolated occurrence is shown by an x-ray film of another case [Fig. 8], in which fracture occurred through one of the points of partial separation. Other points of infraction are indicated by the arrows.)

Physical examination in June, 1939, revealed the typical picture of Paget's disease, with great enlargement of the head, marked overgrowth of the jaws and enlargement of the left clavicle and both femurs. The blood pressure was 155/95. There were present a basal systolic murmur and a thrill that were interpreted as aortic stenosis on an arteriosclerotic basis. The serum calcium level was 10 mg. per 100 cc. The urine contained a moderate amount of calcium, and the sediment showed 10 to 15 white cells per high-power field.

The patient was advised to take 1 glass of milk and 10 drops of viosterol three times a day. She was seen at about

yearly intervals thereafter. The blood-chemistry findings at these visits are given in Figure 9 and Table 2. In November, 1941, a urine examination showed a specific gravity of 1.030, no albumin, a moderate amount of calcium and 20 to 30 red cells and 4 to 6 white cells per high-power field. At that time the milk intake was reduced to 2 glasses a day and the viosterol intake was decreased to 10 drops twice a day. In addition, sodium citrate, 2 gm. three times a day, was prescribed.

On November 19, 1942, the urine showed a specific gravity of 1.002, no albumin and 2 red cells and 4 white cells per high-power field. The serum calcium was 10.4 mg. per 100 cc., the serum phosphorus 4.0 mg. and the serum phosphatase 28.0 Bodansky units.

On December 28, the patient slipped on the floor and fractured her right femur at the junction of the middle and distal third. She was admitted to the Baker Memorial Hospital under the care of Dr. George W. Van Gorder.* X-ray examination showed the fracture fragments to be in satisfactory alignment; hence no orthopedic procedures were instituted except simple traction (Fig. 7B).

The course thereafter is shown in Figure 9 and Table 2. Because of the experience in Case 1, milk was omitted from the diet from the time of admission, and other fluids by mouth were forced so far as possible. The patient remained comfortable for the first 5 weeks. Then, as the serum calcium began to rise, she complained of anorexia and dryness in the nose and throat, with difficulty in swallowing. This was followed by constant nausea and vomiting. The fluid intake became inadequate. For the next 3 weeks, during the period of maximal hypercalcemia, the patient was given almost daily an intravenous infusion of 1000 to 2000 cc. of equal parts of 5 per cent dextrose and normal saline solutions. On February 8, 1943, when the serum calcium level had fallen to 11.1 mg. per 100 cc., the intravenous infusions were discontinued. At the same time the gastric and pharyngeal symptoms practically disappeared, and thereafter the patient was able to maintain an adequate fluid intake by mouth.

X-ray films taken on January 18, 1943 (Fig. 7C), 21 days after the fracture, showed that the alignment had been maintained and that a marked amount of calcified callus was already present. The bone healed so rapidly that by the first week in February the traction could be removed, and by February 15 the patient was able to get out of bed. The subsequent course was uneventful.

DISCUSSION

Pathologic Physiology of Paget's Disease

The pathologic lesions of Paget's disease have been discussed; it remains to attempt an interpretation. It is clear that the initial lesion is a localized factor causing bone destruction, which has no respect for structural requirements. The bone destruction renders the involved bone more susceptible to stresses and strains. To compensate for this, the osteoblasts are stimulated to lay down more matrix; the serum phosphatase level — an index of osteoblastic activity — therefore rises. When the stresses and strains are constantly present (in the vertebrae and long bones), bone repair occurs almost simultaneously with bone destruction; when stresses and strains are minimal, as in the skull, bone repair may lag behind bone destruction (see above).

In the meantime, the localized destructive factor persists and continues to destroy bone, including some that has been newly laid down as a reparative process. The joints between new and old bone are

*We are indebted to Dr. Van Gorder for his co-operation in the study of this patient.

TABLE 2. Chemical Determinations in Case 2.

DATE	BLOOD SERUM LEVELS					URINE			REMARKS
	CALCIUM mg./100 cc.	PHOSPHORUS mg./100 cc.	PHOSPHATASE Bodaniky units	PROTEIN mg./100 cc.	NONPROTEIN NITROGEN mg./100 cc.	CALCIUM QUASI-QUANTITATIVE TEST*	CALCIUM QUANTITATIVE TEST†	SPECIFIC GRAVITY	
6/ 3/39	10 0	—	—	—	—	++	—	—	17 KETO- STEROIDS mg./24 hr.
11/18/40	10 4	4.2	42.2	—	—	—	—	—	Classic Paget's disease; 3 glasses of milk and 30 drops of viosterol given daily.
11/ 5/41	—	3.8	36.2	—	—	++	—	—	—
11/19/42	10 4	4 0	28 0	—	—	—	—	1 030	Increased bowing of femurs; sodium citrate, 6 gm. daily.
12/28/42	—	—	—	—	—	—	—	1 002	—
12/30/42	10 1	3 7	41 9	5.9	—	—	—	—	Fracture, leg in traction; milk stopped and water forced.
12/31/42	—	—	—	—	—	—	—	1 024	No complaints
1/ 6/43	11 5	5 5	24 4	4 7	—	++	—	1 020	No complaints
1/11/43	11 9	4 1	31 4	8 0	—	++	—	1 009	No complaints
1/18/43	13 9	4.2	18 8	—	43	++	—	1 015	Anorexia and dysphagia
1/22/43	13 5	3 4	13 4	—	33	++	434	1 016	Nausea and vomiting; fluids given by vein.
1/26/43	13 9	3 6	13 3	—	—	++	—	1 012	Nausea and vomiting; fluids given by vein.
2/ 1/43	13 0	4 0	16 5	—	—	—	—	—	Nausea and vomiting; fluids given by vein.
2/ 8/43	11.1	3 4	16 9	5 7	—	—	519	—	Patient somewhat better
2/15/43	11 6	3 9	20 1	5.4	—	++	296	1 010	Intravenous infusions stopped
2/23/43	10 4	3 0	21 4	—	—	+	—	1 010	Patient much better
3/ 1/43	10.7	4 1	31.4	6 7	—	++	112	1 010	No complaints
3/ 8/43	9 9	3.2	24 6	6 1	14	0	—	—	Traction removed; patient up in chair.
3/15/43	10 7	3 8	34 8	6 1	18	++	—	1.027	Improvement continuing
3/22/43	9.4	3 5	35 5	7.1	16	+	—	1 008	Patient walked a few steps with brace
3/29/43	11.5	3 5	41 5	8 2	22	+	38	1 006	Improvement continuing

*Solkowitch test.

marked by cement lines; in the constant battle between bone destruction and bone repair many such lines arise. Since the local destructive factor has no respect for the mechanical requirements of the skeleton, the lines have no order, hence the mosaic structure (see arrows in Fig. 2A). There results a bone of poor architectural value. This factor explains three of the striking clinical characteristics of the disease: the marked tendency to overgrowth of bone, the fact that the serum phos-

patients herein cited showed hypercalcemia and some evidence of decreased renal function.

Case 2 illustrates well the sequelae of immobilization in a patient with Paget's disease. The serum phosphatase fell from 42 to a low of 13 Bodansky units; the serum calcium gradually climbed from 10.1 to a high of 13.9 mg. per 100 cc., this high point coinciding with the low point on the phosphatase curve. The daily calcium excretion in the urine reached 519 mg. When activity was resumed the

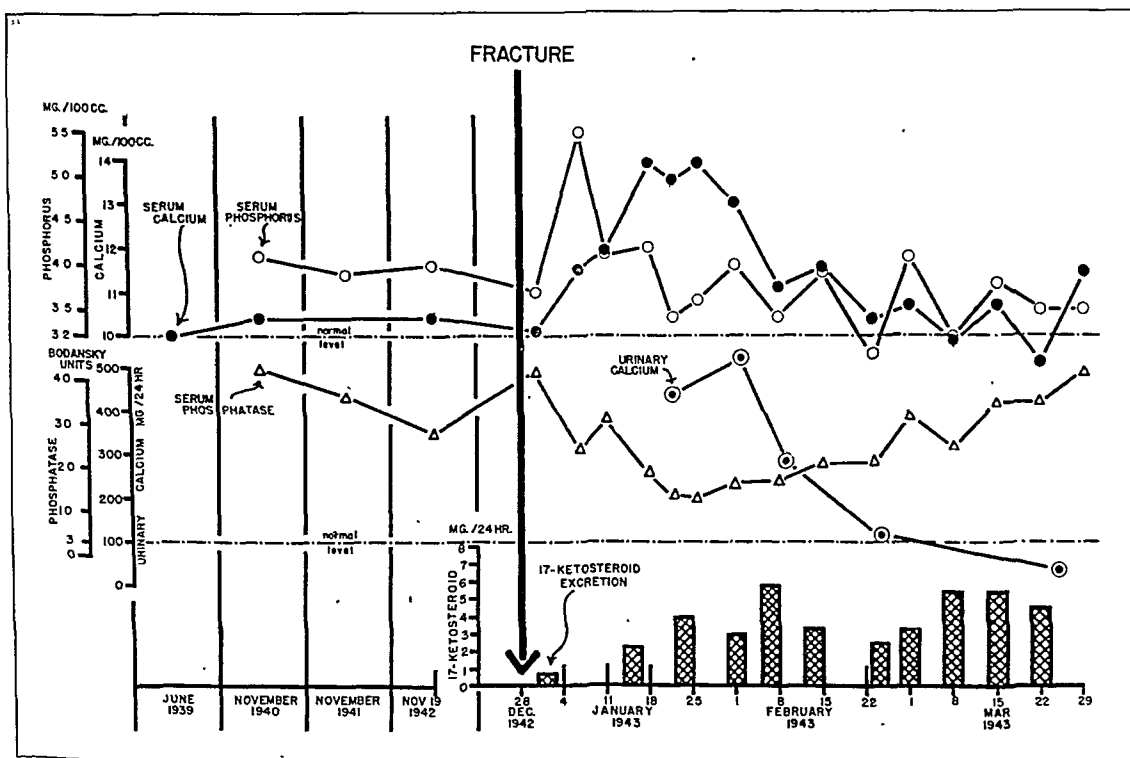


FIGURE 9. Chart Illustrating the Effect of Fracture on the Serum Calcium, Phosphorus and Phosphatase Levels and on the Urinary Excretion of Calcium and 17-Ketosteroids in Paget's Disease (Case 2).

phatase level, — an index of bone repair, — is so high per unit of diseased bone and the tendency of bones to become deformed in spite of marked overgrowth — for example, bowed femurs.

In Figure 10 the sequence of events is illustrated schematically.

Effect of Immobilization on Paget's Disease

When a bone containing Paget's disease is immobilized, the stimulus for bone formation ceases; and bone destruction continues unabated. There results a decrease in the serum phosphatase level and in bone mass and an increase in the urinary excretion of calcium (Fig. 10B). There may even be hypercalcemia when the amount of calcium to be excreted exceeds the ability of the kidney to excrete it (Fig. 9) or when the kidney function becomes impaired from hypercalciuria. Thus, both

values returned to the prefracture levels, the daily calcium excretion in the urine falling to 38 mg.

Possible Role of the Alarm Reaction

The decreased formation of bone in Case 2 was probably not entirely due to immobilization. As with any injury,⁷ there was a depression of the urinary 17-ketosteroid excretion, with a return to a normal value for a patient of this age with recovery — from 1.7 mg. in twenty-four hours on the third day after injury to 5.5 mg. on the seventy-seventh day. It is quite probable that not only this change in the 17-ketosteroid excretion but also part of the depression in bone formation are to be attributed to an alteration of adrenocortical function that is common to all injuries (compare the so-called "alarm reaction" of Selye⁸). The net result of this altered function following injury is a

curtailment of tissue formation except at the site of injury.⁵ Ordinarily such a curtailment may be overlooked, but in Paget's disease, where bone formation is rapid and extensive, any influence that suppresses it is magnified.

It should be noted that this curtailment of tissue anabolism following injuries does not affect the

good callus was being put down at the site of the injury.

Dangers and Their Prevention

When a patient with Paget's disease is immobilized, the danger of a so-called "chemical death" exists. Thus, the patient in Case 2, if treated in

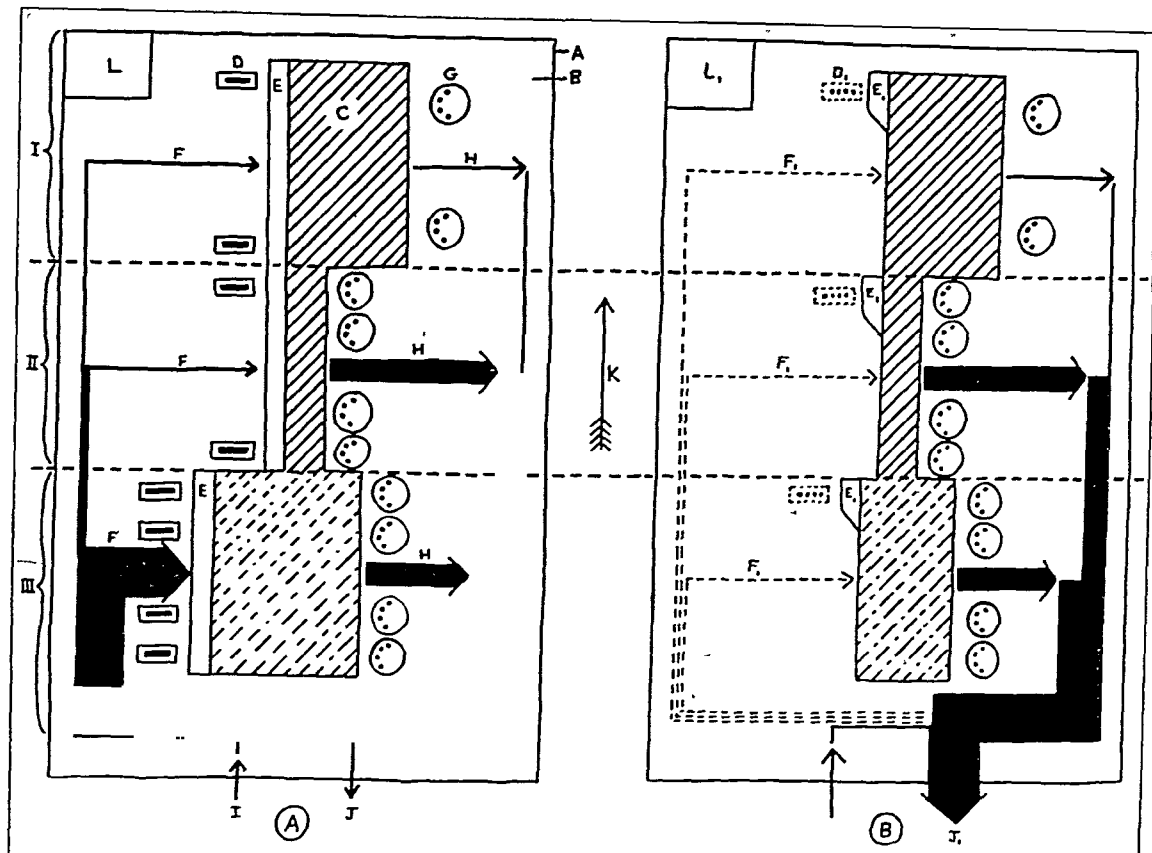


FIGURE 10. Schematic Diagrams Showing the Processes in Uncomplicated Paget's Disease (A) and in Paget's Disease after Immobilization (B).

Three stages or zones are depicted: I, normal bone; II, bone destruction; III, bone destruction with compensatory repair.

UNCOMPLICATED PAGET'S DISEASE. The designations are as follows: A — body limits; B — body fluid; C — bone mass having three surfaces (one where nothing is happening, one where bone is being resorbed, and one where it is being laid down), D — osteoblast laying down a matrix of osteoid tissue (E); F — arrow indicating by its size the rate of deposition of calcium and phosphorus; G — osteoclast; H — arrow indicating by its size the rate of resorption of calcium and phosphorus; I — calcium and phosphorus entering the body through the gastrointestinal tract; J — calcium and phosphorus leaving the body by the kidneys and other exits; K — arrow indicating the direction of advancement of the disease process. In Zone II, note the decrease of the bone mass, the increase of osteoclasts and the increase in the rate of resorption of calcium and phosphorus. In Zone III, note that the increased stresses and strains from the decreased bone mass in Zone II have resulted in an increase of osteoblasts, an increase in the rate of deposition of calcium and phosphorus and an increase in bone mass, which is of poor quality. Analyses of the serum (L) show a normal calcium level, a slightly elevated phosphorus level and a markedly elevated phosphatase level.

PAGET'S DISEASE AFTER IMMOBILIZATION. The osteoblasts (D_i) are hypoplastic owing to loss of the stimulus of stresses and strains through immobilization; this results in a decrease of matrix (E_i) and a decrease in the deposition of calcium and phosphorus (F_i). In Zone III note that the huge amount of compensatory bone formation (F) is no longer present because of immobilization. Since bone destruction (H) continues unabated, there results not only a marked diminution of the bone mass (C) but also a tremendous increase in the excretion of calcium and phosphorus in the urine (J_i). Analyses of the serum (L_i) show a markedly elevated calcium level, a slightly elevated phosphorus level and a phosphatase level that is still slightly elevated.

anabolism at the site of the injury. It is not unlikely that there is some local factor that causes maximal tissue repair there. Thus in Case 2, while the rest of the femur was melting away, a

the ordinary fashion with liberal amounts of milk, no special regard for fluid intake and more than minimal immobilization, might well have developed an even higher blood calcium level, anuria and

death. Metastatic calcification in the lungs might have been overlooked at autopsy and the cause of death put down as bronchopneumonia. To control the hypercalcemia and hypercalciuria, all that is needed is a low-calcium diet and sufficient fluid by vein if need be so that the serum and urinary calcium concentrations do not rise to dangerous levels. Immobilization should be kept at the absolute minimum, and mobilization should be begun as early as possible, not only to avoid chemical death but to avoid extreme atrophy of the bones (Fig. 5C).

A Possible New Symptom of Hypercalcemia

Besides nausea and vomiting, which are recognized symptoms of hypercalcemia, both the patients herein cited experienced a peculiar sensation of dryness in the nose and throat, with difficulty in swallowing. These symptoms seemed to be associated with the hypercalcemia. The patient in Case 1 was treated for "sinusitis" for several weeks before the probable role of the hypercalcemia in producing these symptoms was appreciated.

SUMMARY AND CONCLUSIONS

The bone lesions of Paget's disease are not generalized but spotty in their distribution. This fact alone is strong evidence against the disturbance being on an endocrinologic or metabolic basis.

The initial lesion in Paget's disease is bone destruction, the cause of this being entirely obscure. The resultant weakness of the involved bones renders them less resistant to stresses and strains, and this leads to a stimulation of the osteoblasts and an overproduction of bone. In the skull, where there are fewer stresses and strains, one frequently encounters bone destruction divorced from the overproduction of bone (so-called "acute Paget's disease of the skull").

The repair of bone by the osteoblasts is never completed, since the localized initial disorder causing bone destruction apparently persists. There results alternating destruction and repair of bone, which eventually leads to the pathognomonic pathological finding, the so-called "mosaic structure." This mosaic appearance is due to the highly irregular cement lines, each one of which demarcates a place where bone destruction temporarily ceased and bone repair began.

The increased bone destruction and bone repair seen in the lesions of Paget's disease are closely

similar to those seen throughout the skeleton in the osteitis fibrosa generalisata of hyperparathyroidism. There is one important difference, however: in osteitis fibrosa generalisata, that bone is destroyed that can best be spared; in Paget's disease, bone is destroyed without regard to structure. This accounts for the complete lack of arrangement in the cement lines (see above), and for the fact that the bones in Paget's disease are extremely pliable in spite of marked overgrowth of bone.

If a bone containing Paget's disease is immobilized as after a fracture, the following events occur: A lack of stress and strain, in all probability abetted by the alarm reaction of Selye, curbs the overactivity of the osteoblasts, and the serum phosphatase level, an index of bone formation, falls. The initial disturbance causing bone destruction persists. There results a marked imbalance between bone destruction and bone formation. The increased calcium and phosphorus coming from the bone leads to hypercalciuria and hyperphosphaturia. The capacity of the kidney to excrete calcium may be overtaxed, with a resulting hypercalcemia; if fluids are not forced, if the diet is not kept low in calcium and if immobilization is not kept at a minimum, a so-called "chemical death" from hypercalcemia may supervene.

Studies are cited of 2 patients with Paget's disease who sustained fractures. The above chain of events, up to and including the hypercalcemic stage, took place.

Although, in Paget's disease, the broken bone becomes decalcified as a whole, the fracture site shows a rapidly forming and calcifying callus. This is best explained by the hypothesis that some local influence stimulating osteoblasts is set loose at the site of the fracture.

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EOSINOPHILIC INFILTRATION OF THE LUNGS (LOEFFLER'S SYNDROME)*

STEWART H. JONES, M.D.,† AND CARLTON R. SOUDERS, M.D.‡

BOSTON

IN the differential diagnosis of pulmonary disease Loeffler's syndrome should be remembered. It has been mistaken for tuberculosis,¹ bronchiectasis and neoplasm, and probably explains many so-

and the fatigue for 2 months. The cough was only slightly productive, was worse at night than in the daytime, and was associated with sufficient wheezing so that ephedrine had been prescribed. At times she had a sharp pain of short duration in the right side of the lower thorax, and a "tired feeling" in the lumbar region. She had had similar, but milder, attacks each autumn for the preceding 2 years, but had not felt ill enough to consult a physician.

On physical examination the patient was found to be underweight but did not appear to be ill. The only significant signs were in the upper lobe of the left lung, where the resonance was impaired and sibilant rales were present.

Roentgenograms of the chest showed an infiltration extending out from a large left hilar shadow into the mid-lung and reaching the periphery in the second intercostal space anteriorly (Fig. 1). A pneumonic consolidation or neoplasm was suspected. Examination of the lungs by fluoroscopy suggested the possibility of tuberculosis.

Hematologic examination revealed a marked eosinophilia, which with other findings is shown in Table 1. Hemoglobin determinations, red-cell counts and urine analyses were normal. To discover a possible cause of the eosinophilia the following tests, the reactions to all of which were negative, were done: sputum examination for tubercle bacilli, a patch test with tuberculin, the giving of eighteen inhalant and food allergens endermically, examination of two warm stools for amebae and ova, agglutination tests for brucellosis,

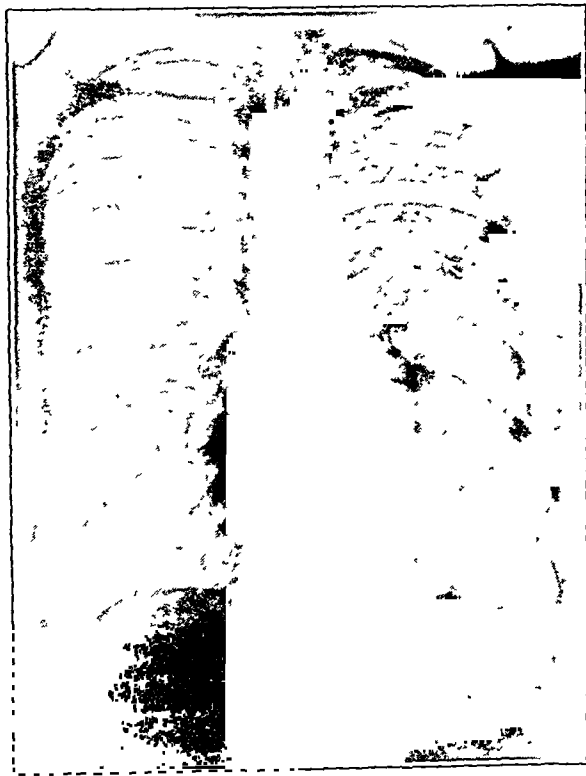


FIGURE 1. Roentgenogram of Chest Taken October 21.

called "abortive" pneumonias, as well as the frequent infiltrations seen in roentgenograms of the lungs of patients with bronchial asthma.

Loeffler² first described this condition in 1932 and presented 37 cases. Since then a small number of cases has been reported, both in children and in adults, by various authors in many languages. A recent fluoroscopic examination of 6283 men discharged from Army service revealed abnormalities of the lungs in 55.³ In 13 of these the diagnosis was eosinophilic infiltration.

CASE REPORT

A 33-year-old, married Negress came to the Lahey Clinic on October 21, 1943, complaining of cough and fatigue. She had always lived in the vicinity of Boston, and worked as a private secretary. The cough had been present for 2 weeks



FIGURE 2. Roentgenogram of Chest Taken October 27

and an intracutaneous test with brucellergin (0.1 cc, undiluted), and an intracutaneous test for trichinosis.

The patient continued to rest at home, but was not ill enough to remain in bed. On October 27, a roentgenogram showed some diminution in the lung shadow (Fig. 2), and by December 7 the shadow had completely disappeared (Fig. 3). At that time she no longer coughed, had gained

*From the Department of Internal Medicine, Lahey Clinic.
†Member, Department of Internal Medicine, Lahey Clinic.
‡Member, Department of Internal Medicine, Lahey Clinic (on leave of absence).

3 pounds in weight and felt well enough to return to work. On examination a month later, no abnormal signs or symptoms were present.

DISCUSSION

Since no deaths as a result of Loeffler's syndrome have been reported, the nature of the pathologic



FIGURE 3. Roentgenogram of Chest Taken December 7

changes that occur in the pulmonary tissues is unknown. Its cause is likewise unknown, although allergy is suspected from its frequent association with vasomotor rhinitis and asthma and its occasional occurrence in persons with an allergic family

parasites, such as *Fasciola hepatica* and *Ascaris lumbricoides*, have been found.^{4,6} A seasonal incidence of this disease was recorded in China by Engel⁷ who found that cases occurred during May and June while the privet plant was pollinating. Loeffler's cases occurred in July and August. That allergy to the tubercle bacillus may be the cause has been suggested, but Loeffler found positive tuberculin tests in only 13 of 37 adults, and only 1 of these subjects subsequently developed tuberculosis. Smith⁸ has reported a case of Loeffler's disease followed by severe asthmatic symptoms.

A possible relation with brucellosis has been suggested in two cases⁹ in which there were pulmonary infiltrations accompanied by an eosinophilia and definite evidence of brucellosis.

Eosinophilia thus tends to favor the allergic hypothesis. Ten to 60 per cent of the leukocytes are usually eosinophils, and often the highest count is reached when the infiltration is disappearing. Eosinophilia may persist for variable periods,¹⁰ and in one patient lasted for nine months. There is no parallelism between the degree of pulmonary infiltration and the eosinophil count. Eosinophilia is not essential for making the diagnosis, since it may be absent or be depressed by associated infection. More important for diagnosis are concomitant allergic manifestations.

The patient frequently complains of a metallic taste, cough, wheezing and malaise. He does not feel or appear ill. The temperature may be slightly elevated; diminished resonance with sibilant rales may be heard over the areas of consolidation, and blood examination may show leukocytosis, eosinophilia and an increased rate of sedimentation of the erythrocytes. In contrast to the paucity of signs and symptoms are the roentgenographic changes.

Breton¹² described the shadows in the roentgenograms of the lungs as appearing rapidly, disappearing in three to eight days and reappearing elsewhere in the lungs. Fine star-shaped scars were said to

TABLE 1 Summary of Data

DATE	WHITE-CELL COUNT x10 ³	DIFFERENTIAL COUNT						SEDIMENTATION
		EOSINOPHILS %	NEUTROPHILS %	BAND FORMS %	LYMPHOCYTES %	MONOCYTES %	BASOPHILS %	RATE mm per hr
10/21/43	10,350	48.5	33.0	1.0	13.0	3.5	1.0	31.0
10/27/43	10,150	—	—	—	—	—	—	42.0
11/18/43	8,400	27.0	48.5	0.5	20.0	4.0	0.0	—
12/ 6/43	6,500	9.0	57.0	0.0	31.0	3.0	0.0	8.0
1/ 5/44	6,300	9.0	41.0	0.0	40.0	10.0	0.0	15.0

background. Various substances have been considered as allergens. In one patient¹ symptoms and roentgenographic findings persisted for four months until amebae were eliminated from the stool. Another patient⁵ had amebae in the sputum but not in the stool, and both the lung infiltration and the accompanying asthma disappeared after emetine therapy. Other

result. Loeffler¹ observed the pulmonary densities to be single or multiple, unilateral or bilateral, and clearly or irregularly outlined, and in some cases to be indistinguishable from pulmonary tuberculosis.

SUMMARY

A case of Loeffler's syndrome has been presented with a discussion of its significance, cause, symp-

toms and diagnosis. As possible causes the following were considered and rejected: tuberculosis, infestation with amebae or other intestinal parasite, brucellosis and trichinosis. The syndrome appears to be a manifestation of allergy, the cause of which is unknown.

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PENICILLIN SODIUM THERAPY IN EXPERIMENTAL WEIL'S DISEASE*

DONALD L. AUGUSTINE, Sc.D.,† DAVID WEINMAN, M.D.,‡ AND JOAN McALLISTER, M.A.§

BOSTON

REPORTS from different sources¹⁻³ have conclusively shown the value of penicillin in the treatment of relapsing fever and rat-bite fever in animals. Its remarkable therapeutic value in these two spirochetal diseases suggested that similar action of the drug could be expected in the treatment of infectious jaundice. The following experiments were performed to gain information on this question.

Our strain of *Leptospira icterohaemorrhagiae* was obtained in January, 1944, from Dr. Martin Frobisher of the Johns Hopkins University School of Hygiene and Public Health. It had been freshly isolated from a human infection and was highly virulent for guinea pigs. Prior to the present experiments it was maintained for several weeks in our laboratory by passage in guinea pigs. The infected animals usually developed jaundice on the fourth to the sixth day and died before the seventh day after infection. White guinea pigs, weighing approximately 180 gm each, were used for the tests. The penicillin sodium was furnished by Dr. Chester S. Keefer. Two experiments were performed.

Experiment 1 Ten guinea pigs were inoculated intraperitoneally with 1 cc of a suspension of macerated livers and kidneys from other infected animals. Dark-field examinations showed the inoculum to be rich with spirochetes. On the fourth day after infection the entire lot showed varying degrees of jaundice. Five animals in which jaundice was particularly pronounced were selected for treatment. The remaining 5 guinea pigs served as controls. The treated animals received intraperitoneally 4000 Oxford units of penicillin in 1 cc of saline solution every four hours for seventy-eight hours, or until death occurred.

The first death was that of one of the treated guinea pigs, which had received 4000 units of penicillin. Two more of the treated animals died after having received 8000 units of the drug, and the remaining 2 treated animals were

found dead on the morning following the last treatment or after having received the total dose of 48,000 units. All the untreated controls died prior to the death of the 2 guinea pigs that received 48,000 units of the drug. At autopsy, both treated and untreated animals showed similar and characteristic lesions, with motile leptospira in fresh preparations of the liver and kidneys.

From the results obtained from this experiment it appeared that either penicillin was inactive against *L. icterohaemorrhagiae* or that the disease had progressed to such an extent before treatment was begun that any action the drug might have had against the organism did not alter the course of the disease.

Experiment 2 Eight guinea pigs were inoculated with *L. icterohaemorrhagiae*, as in the previous experiment, but treatment was begun before objective symptoms of the disease became apparent. Thirty-eight hours after the inoculations were made, treatment of 4 of the animals was instituted. Each of the treated animals received intraperitoneally 5000 units of penicillin sodium in 1 cc of saline solution every four hours for forty-eight hours. The total dose received by each guinea pig was 60,000 units.

Jaundice was evident on the third day of infection in all the untreated controls. Three of the controls died, one on the third and two on the seventh day after inoculation. At autopsy these animals showed characteristic lesions of Weil's disease. The fourth control, which appeared to have recovered, was sacrificed on the fifteenth day after inoculation. The internal organs appeared normal. No spirochetes were found in several fresh specimens of the liver, lungs and spleen, but a few were seen in preparations of the kidneys.

None of the treated animals developed apparent jaundice or other signs of illness except slight roughness of fur. One of the animals was found dead on the morning of the fourth day after completion of the treatment. Another was found dead on the fifth day, and a third died on the seventh day after final treatment. Thus, deaths among the treated lot of guinea pigs occurred on the eighth, ninth and eleventh days after inoculation. At autopsy *L. icterohaemorrhagiae* was demonstrated in the liver and kidneys of each of these guinea pigs, but there were no severe lesions. The roughness of fur on the last guinea pig was of a transient nature, and by the tenth day after inoculation it appeared normal. It was sacrificed on the eleventh day after final treatment, or the fifteenth day after infection. All organs appeared normal. No spirochetes were seen in several fresh preparations of the liver, kidney, lungs and spleen.

*From the Department of Comparative Pathology and Tropical Medicine, Harvard Medical School and Harvard School of Public Health.

†Associate professor of comparative pathology and tropical medicine, Harvard Medical School and Harvard School of Public Health.

‡Instructor in comparative pathology and tropical medicine, Harvard Medical School and Harvard School of Public Health.

§Assistant in comparative pathology and tropical medicine, Harvard School of Public Health.

In this experiment there is evidence that penicillin had some suppressive effect but was not curative.

The results of a series of experiments by Hamre et al.⁴ show that the acute toxicity of penicillin in guinea pigs, mice and rabbits is low; however, daily dosages of 7000 to 12,000 units per kilogram of body weight given subcutaneously over a period of several days caused the death of guinea pigs but not that of mice or rabbits. When guinea pigs were treated with the same dose of penicillin per kilogram as that given to man, they did not die and failed to show any signs of toxicity. It is therefore possible that the death of the treated guinea pigs was due to toxicity of the drug rather than to the experimental infection. The fact that the treated animals in the second experiment did not die until four to seven days after treatment had been stopped indicates that the drug was not the cause of death.

* * *

Our findings are not in accord with those of Heilman and Herrell,⁵ who report no deaths from the disease in 32 guinea pigs treated with penicillin and a mortality rate of 91 per cent in an equal number of untreated controls. This difference may be attributed to the early administration of peni-

cillin — seventeen to twenty-four hours after inoculation — and to the use of a strain of *L. icterohaemorrhagiae* with relatively low virulence.

From these results it is apparent that penicillin has a suppressive effect on the organism in a highly susceptible host when given before the appearance of clinical manifestations. This observation suggests that the early use of penicillin might alleviate the symptoms of Weil's disease in man, in whom the disease has a relatively low fatality rate. The value of penicillin in practice, however, is questioned. Its early administration might be effective in preventing the disease, but in the present experiments, it had no curative value after the appearance of clinical manifestations.

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Correction. In the article "Phenarsine Hydrochloride in the Treatment of Syphilis" by Drs. W. F. Boardman and R. Kaldeck, which appeared in the January 6, 1944, issue of the *Journal*, the figures given in Table 2 for the dosage of phenarsine are erroneous. The "thousands" represent the number of doses, and the "hundreds" the dosage in milligrams. In other words, in Case 1 six doses totaling 200 mg. were given, in Case 2, seven doses totaling 300 mg. and so forth.

MEDICAL PROGRESS

THORACIC SURGERY

JOHN W. STRIEDER, M.D.*

BOSTON

THE publication of this review during the sixth year of the war finds many of the world's outstanding thoracic surgeons in the armed forces of their respective countries, and an increasing proportion of a diminishing literature concerned with the surgery of trauma and of war.

Surgery has been called the child of trauma, and it is generally considered that the experiences gained in World War I furnished the impetus that resulted in the precocious development of thoracic surgery, the youngest child of surgery, during the ensuing quarter of a century. Undoubtedly much that will be learned of the surgery of trauma of the chest in this war will be valuable in the highly mechanized peacetime that lies ahead. Even now, for example, there is a better understanding of the principles involved in the treatment of so commonplace a complication as traumatic hemothorax and its sequelae.

There remains, however, a considerable body of literature that deals with the problems of civilian practice, many of which, as is the case in pulmonary tuberculosis, will be greatly augmented by the ravages of war. Other problems, such as bronchogenic carcinoma, are of increasing importance simply because they are integrated with the natural history of the human race. It is with these and other similar aspects of thoracic surgery that this review concerns itself.

TUBERCULOSIS

Lobectomy

Within very recent years, and with the perfection of the technics of lobectomy and pneumonectomy, many thoracic surgeons who deal with pulmonary tuberculosis have manifested a renewed interest in the application of these procedures to the surgical treatment of this disease.

During the early developmental period of the surgical treatment of phthisis, the actual removal of that portion of a lung containing tuberculous lesions was considered an attractive possibility by various clinicians. Thus, Alexander¹ states that Tuffier performed such an operation in 1891; an indurated tuberculous area in an upper lobe was resected through an incision in the anterior second intercostal space. Seven years later the patient was apparently cured but died of grippe. Up to 1921, however, Tuffier and Jessen had collected less than a dozen cases in which tuberculous pulmonary tissue had been successfully removed, and

about as many in which the operation was fatal or otherwise unsuccessful.

In 1935, Freedlander² reported a case in which he performed lobectomy for a persistent cavity in the right upper lobe. The patient was alive and well as reported by him³ in May, 1944. In 1939, Jones and Dolley⁴ reported two cases of lobectomy and two pneumonectomies for pulmonary tuberculosis. All the patients survived the operations. These results were considered encouraging. In 1940, Dolley and Jones⁵ reviewed their previously reported cases and added 3 more. In the discussion of this paper many surgeons added small series of cases in the aggregate of which the over-all mortality was discouraging. Thus, of 19 patients treated by total pneumonectomy, 8 (40 per cent) died and of 31 treated by lobectomy 8 (26 per cent) died. In 1942, Thornton and Adams⁶ collected and analyzed the reported cases of lobectomy and pneumonectomy. There were 29 cases of pneumonectomy with a mortality of 45 per cent and only 41 per cent satisfactory results. There were 46 cases of lobectomy with a mortality of 26 per cent and 69 per cent satisfactory results. It may be presumed that the majority of the operations were performed by the tourniquet technic. In this series, the most frequent complications were persistent fistula, contralateral spread and empyema. The most frequent indications were tuberculoma, tuberculous bronchiectasis, bronchial stenosis and the persistence of a cavity after thoracoplasty.

It is of interest to note that during this period of discouragement, and at the same meeting of the American Association for Thoracic Surgery in 1940 at which Dolley and Jones reviewed their results, Blades and Kent⁷ reported 10 successful cases of lobectomy for nontuberculous disease (9 of bronchiectasis and 1 of mixed tumor of the bronchus) in which were employed the technic of intrahilar dissection and individual treatment of each hilar structure of the lobe. This splendid contribution followed closely on the pioneer work of Rienhoff⁸ on pneumonectomy for malignant disease by individual ligation and of Crafoord,⁹ Churchill,¹⁰ and Churchill and Belsey,¹¹ the last paper offering new theories of segmental pneumonectomy that had hitherto been only vaguely conceived. It is reasonable to say, then, that a new era in the treatment of pulmonary disease had been entered on.

Up to that time surgical extirpation of the lung or one of its lobes had been accomplished by the use of a tourniquet with mass ligation of the hilar portion of the lung or lobe, as performed by Haight¹² and Graham.¹³ Later, after the manner of Shen-

*Assistant professor of thoracic surgery, Boston University School of Medicine; visiting surgeon in charge of thoracic surgery, Massachusetts Memorial Hospitals; visiting surgeon for thoracic surgery, Boston City Hospital.

stone and Janes,¹⁴ who employed a snare threaded with cord to control the hilus of the lobe, the remaining pedicle after amputation of the lobe could be made smaller and hemostasis effected by placing sutures in the presenting cut surface. Shenstone and Janes performed their lobectomies in one stage, as had Brunn¹⁵ in 1929, when he reported 6 cases with 1 death. This technic, although a milestone in the progress of the attack on the problem, was at best unsatisfactory and unsurgical, since it left masses of devitalized and necrotic tissue in the pleural cavity. Moreover, in the case of pulmonary tuberculosis, tuberculous foci were of necessity traversed during the resection of the pulmonary tissue, with the almost inevitable sequelae of tuberculous empyema or bronchopleural fistula and mixed-infection empyema. Frequently the patient was left with a chronic draining chest sinus, secretions from which were often laden with tubercle bacilli. With the spontaneous opening of a bronchopleural fistula during the postoperative course, bronchogenic spread of the disease in the same or the contralateral lung was of a high order of frequency.

With the proved value of the individual ligation technic, the incidence of these hazards was reduced. In most cases it was no longer necessary to transect tuberculous foci or to leave masses of devitalized tissue to serve as a source of infection within the pleural cavity. The hilar vessels could be individually ligated, forestalling postoperative hemorrhage, and the bronchus closed primarily and covered with pleura or buried in surrounding vital tissue, obviating to a large extent the frequently fatal complication of bronchopleural fistula. Moreover, the hilus of the tuberculous lung was found to be relatively free of the fibrosis that is present in suppurative disease, and the intrahilar dissection could be carried out with comparative ease.

In 1943, Churchill and Klopstock¹⁶ reported 6 cases of pulmonary tuberculosis in which modern lobectomy had been performed. All the patients survived the operation and were either well or greatly improved at the time of the publication of the report. These authors make it clear that they propose lobectomy as a highly selective measure for dealing with certain unilobar lesions. They believe it to be far more conservative of pulmonary function than is even a seven-rib thoracoplasty. Since, however, lobectomy is by definition irreversible, it can be suggested as an alternate to artificial pneumothorax only when tuberculosis has produced irreversible or irreparable destruction of lung substance.

In 3 of these cases, lobectomy was performed as a definitive operation where, up to that time, thoracoplasty might have been the operation of choice. In one of the patients, a twenty-two-year-old woman, tuberculin tests (1:50,000 and 1:20,000 dilutions of old tuberculin) were negative one month after operation. In view of the fact that pulmonary

tuberculosis is generally considered to have bilateral dissemination, even though microscopic, the implications of such a result could be significant only if many similar cases should be reported and stronger doses of tuberculin be used. Although the total eradication of all foci has been the will-o'-the-wisp pursued by phthisiologists ever since tuberculosis of the lung was recognized as an entity, its accomplishment by surgical means will in most cases probably be purely fortuitous.

At the twenty-fifth annual meeting of the American Association for Thoracic Surgery in May, 1944, several papers were presented that evoked considerable discussion of this important aspect of the surgical treatment of pulmonary tuberculosis. There were many technical issues involved that need not be reported here. Janes¹⁷ analyzed the data in 16 cases of lobectomy that he had performed since September, 1941. The most frequent indication was an open cavity with positive sputum. The upper lobe was affected in 7 cases, the middle lobe in 1, and the lower lobe in 9. Three patients (19 per cent) had died at the time of the report and 13 were considered clinically well. All these operations were performed by the dissection technic. Maier and Klopstock¹⁸ reported on 16 cases of lobectomy for pulmonary tuberculosis. There was 1 death, a mortality of 6 per cent. This death occurred one month postoperatively and was due to a tuberculous spread in the contralateral lung. Of the 15 living patients, 12 had a negative sputum at the time of the report. These authors laid particular stress on the necessity for excellent intratracheal anesthesia, meticulous operative technic and precise localization of the lesions.

Twenty-three cases in which lobectomy was performed — with two operations in 1 case — were analyzed by Overholt and Wilson¹⁹ in a paper read before the 1944 meeting of the American Trudeau Society. There was 1 death, a mortality of 4 per cent. Five patients (21 per cent) had ipsilateral or contralateral spreads or ipsilateral exacerbation of their disease. There were 21 living patients of the 22 whom the authors classified as "reasonable risks"; and in these cases the prognosis was considered good in 13 (62 per cent), guarded in 7 (33 per cent), and poor in 1 (5 per cent).

Although Chamberlain²⁰ agrees that there is a place for lobectomy in the treatment of pulmonary tuberculosis, he presents his arguments why he believes that modern selective thoracoplasty with its low mortality (2 to 5 per cent) and high rate of sputum conversion (80 per cent) should be the procedure of choice in disease of the upper lobe. He believes that lobectomy should be performed only after failure of thoracoplasty because in his opinion based on bronchspirometric studies, "primary upper lobectomy" excises only the active major focus, thus causing overdilatation of the remaining lobe, which is probably a precursor of emphysema,

may cause reactivation of latent foci in the overdistended lobes, and leaves these foci in a poor state of healing or self-protection.

Maier²¹ takes issue with this point of view. He has been unable to demonstrate serious impairment of respiratory function of the remaining lobe or lobes by bronchspirometric studies, and believes that true emphysema of functional significance does not occur in the remaining lobe. Apparently progressive lowering of the oxygen-consumption curves does not occur.

It can thus be seen that there is considerable difference of opinion regarding primary upper lobectomy as a definitive operation. Thoracoplasty is an operation of known potential and mortality, whereas there is no imposing array of statistics dealing with lobectomy performed in cases in which, up to now, thoracoplasty might have been considered the operation of choice. Until such time as there is a sufficient number of cases to be of statistical significance, and until enough time — possibly five years — has elapsed to evaluate properly the results — any detailed discussion must be regarded as largely philosophical. Certainly, the use of lobectomy in well-selected cases should be continued. The hazard that the procedure will be carried out indiscriminately to achieve rapidly the prestige of numbers, as has happened all too often in the history of the surgical treatment of tuberculosis, is ever present, and should be guarded against with great fortitude so that the procedure will not be condemned before it has had a carefully controlled trial.

But although at the present time it seems that primary lobectomy of the upper lobe is far from the philosopher's stone in the treatment of pulmonary tuberculosis, there are other indications for lobectomy that appear to be fairly well defined but concerning which there is lack of complete accord among phthisiologists and thoracic surgeons. From my own experience with 14 cases — 7 lobectomies and 7 pneumonectomies — and that of others,¹⁶⁻¹⁹ these indications appear to include tuberculoma, tuberculous bronchiectasis, certain tension cavities, particularly of the lower lobe, stenotic lesions of lobar bronchi and residual cavitation when thoracoplasty has failed.

Pneumonectomy

The problem of pneumonectomy in tuberculosis differs radically from that of lobectomy. Churchill and Klopstock¹⁶ state:

Total pneumonectomy cannot be considered an alternative to collapse therapy provided that collapse therapy is applicable to the case under consideration. It is both irreversible and nonselective. It irrevocably and seriously limits any therapeutic procedure that may be needed for the lung of the contralateral side. Circumscribed by strict indications, total pneumonectomy in tuberculosis may be a life-saving operation when no other operation is feasible.

Since total pneumonectomy is in most cases performed with greater facility for technical reasons than is lobectomy, there is undoubtedly a tendency to abandon the former, if planned in a given case, and to resort to the latter when the original lobectomy if persevered in might have been successfully completed. This has obscured the issue in many cases and rendered the evaluation of results even more difficult, since the indication for pneumonectomy did not originally exist.

The most frequent indication for total pneumonectomy in tuberculosis is partial or complete stenosis of the main-stem bronchus, with or without symptoms of obstruction as manifested by toxemia. Thus, Lorge and Dufault,²² reporting 3 cases from the Rutland State Sanatorium, state that in 2 the indication was stenosis of the stem bronchus and that in 1 there was widespread bronchial involvement with clinical evidence of repeated blockage of secretions. There was 1 death, and 1 patient had a not very active lesion in the contralateral lung that appeared six months later but showed evidence of clearing.

Of the 15 total pneumonectomies reported by Janes,¹⁷ 10 were performed for stenosis and in 7 of these there was an uncomplicated recovery. Other indications were tuberculoma, extensive infiltration of the whole lung with cavitation and hemorrhage, and cavitation of the middle lobe with infiltration to the upper and lower lobes. In the total series there were 3 deaths (20 per cent), 10 patients were considered well or fairly well, and in 2 cases the outlook was unfavorable.

In the series of 36 pneumonectomies reported by Overholt and Wilson¹⁹ there were 6 deaths, a mortality of 17 per cent. The authors divide their cases into "desperate risks," of which there were 11 with 5 deaths (45 per cent), and "reasonable risks," of which there were 25 with 2 deaths (8 per cent). In the total series there was a contralateral spread in 4 cases (11 per cent). In 29 of the cases pneumonectomy was performed for extensive multilobar disease that was predominantly unilateral, in 5 for uncontrolled disease following thoracoplasty, in 1 for basal tuberculosis, and in 1 for extensive disease of the upper lobe found at operation to involve the lower lobe as well. There is no detailed analysis of the present status of the entire series, but of the 23 living "reasonable-risk" patients the prognosis was considered good in 18 (78 per cent), guarded in 3 (13 per cent) and poor in 2 (9 per cent).

At the Massachusetts Memorial Hospitals, pneumonectomy has been performed in 7 cases of tuberculosis. The indications were as follows: stenosis of the main bronchus in 2 cases, extensive unilateral disease in which other measures had failed in 3, pneumothorax failure with an unexpandable lung in 1 and pneumothorax failure with the cavity in the lower lobe reopened after three years in 1. There were 3 deaths (43 per cent), all in the group with

extensive unilateral disease, from nontuberculous pneumonia in the remaining lung, surgical shock and extensive tuberculous contralateral spread, respectively.

Alexander²³ states:

The choice between thoracoplasty and pneumonectomy must be based on a number of important factors. If the bronchial stenosis is so great that the patient cannot effectively evacuate the pulmonary secretions by coughing even after attempted bronchoscopic dilatation of the stricture, and consequently becomes increasingly toxic, thoracoplasty would be unduly dangerous because it probably would, at least during the period of the staged operations, further impair the effectiveness of coughing. In such cases, pneumonectomy is the operation of choice and should also be considered if thoracoplasty has already been performed and has left the patient with the symptoms just mentioned. But if there are any active tuberculous lesions in the opposite lung, or if any progressive ulcerative bronchial lesions are present, pneumonectomy is definitely contraindicated. In this event, no surgical treatment, unless possibly direct surgical drainage of a single large tuberculous cavity, could safely be used. There are very few patients who have the clear-cut indications for pneumonectomy and, at the same time, no contraindication.

This sound opinion is probably the one held by the great majority of thoracic surgeons. Although the presence of bronchial stricture undoubtedly makes thoracoplasty more hazardous, Alexander, Sommer and Ehler²⁴ report that 25 patients (66 per cent) in a series of 38 cases have closed cavities and negative sputums and that only 3 (8 per cent) are dead.

As is the case in lobectomy, only time and a careful follow-up will permit an accurate evaluation of the place of pneumonectomy in the treatment of pulmonary tuberculosis.

BRONCHOGENIC CARCINOMA

The increasing frequency with which cancer of the lung has been reported as a cause of death in recent years has aroused considerable speculation whether the increase represents a real change in the incidence of this form of malignant neoplasm or is merely the result of improved methods of diagnosis in combination with a more careful search for a disease that has attracted attention because it is reported more frequently than it has been in the past. Dorn²⁵ states that between 1914 and 1930 the death rate from cancer of the lungs and pleura increased by nearly 400 per cent, as compared with an increase of 20 per cent for all forms of cancer combined. The change among males exceeded that among females, the respective increases being 450 and 260 per cent.

The death rate from cancer of the lungs and pleura continued to increase from 1930 to 1940. Eliminating the changes in the age composition during the past decade, this death rate is shown to have increased by 22 per cent among white females and by 78 per cent among white males, or roughly 2.5 and 8.5 per cent per year, respectively. Nearly 3 per cent of 39,970 patients with malignant neoplasm in the white population of a

study group were reported to have a primary cancer of the lung.

It is estimated that between 450,000 and 500,000 persons in the United States are under treatment for cancer. In approximately 20,000 of the known cases there is a primary cancer of the respiratory system; of these patients about 13,000 are being treated for primary cancer of the lung. Slightly more than 8000 new cases of primary cancer of the lung are diagnosed and receive treatment for the first time each year.

Ochsner and DeBakey²⁶ state that at the beginning of this century the lesion was considered a museum curiosity, but that recently it has been shown that the lung ranks second only to the stomach as the primary site of cancer. This statement is in accord with a ten-year survey of autopsies on carcinoma of the lung by Halpert²⁷ at the Charity Hospital in New Orleans, which reveals both a relative and an absolute increase. During the decade ending December 31, 1940, 12,972 autopsies were performed, 8862 of them on persons over one year of age. Among the subjects there were 135 with carcinoma of the lung, 205 with carcinoma of the stomach, and 66 each with carcinoma of the biliary system and of the pancreas. A year-by-year analysis shows that whereas the incidence of carcinoma of the stomach remained about the same, that of the lung gradually increased and during the last two years *exceeded* that of carcinoma of the stomach.

Blades²⁸ states that at the Barnes Hospital in St. Louis 62 proved cases of bronchogenic carcinoma were seen from 1933 to 1936. During the following three years, 117 patients with bronchogenic carcinoma were admitted for treatment. It thus becomes apparent that the increase in the incidence cannot be attributed to improvements in diagnosis or increased awareness of the condition, but must be considered actual, as demonstrated both by autopsy and by clinical observations.

Although bronchogenic carcinoma occurs most frequently in the age group of fifty to seventy, no age is exempt. It is seen frequently in the thirties and forties, and Hauser²⁹ reports a case in a Negro baby aged seventeen months.

To my knowledge, there has never been an authenticated case of bronchogenic cancer that has been reported as a five-year cure as the result of radiation therapy. Many radiologists,^{30, 31} however, believe that this form of therapy has palliative usefulness and should be employed in certain inoperable cases.

It is now generally recognized that the ideal in the treatment of bronchogenic carcinoma is its surgical extirpation by total pneumonectomy. In rare cases lobectomy may be used, but, as in cancer surgery in general, only by the sacrifice of the entire organ can one hope to achieve the greatest number of cures. Since Graham's¹³ first successful

case in 1933, hundreds of successful pneumonectomies have been performed in the various thoracic clinics throughout the world.

Unfortunately, the vast majority of cases in which this diagnosis is made are inoperable when first seen by the thoracic surgeon. Thus, of 155 cases of primary carcinoma of the lung seen by Churchill³² only 27 (17 per cent) were suitable for resection. In a recent three-week period, I saw 18 patients with proved bronchogenic cancers, only 1 of whom was operable when first seen and on whom pneumonectomy was successfully performed. During 1941 to 1943, approximately 75 cases were diagnosed and 50 proved histologically at the Boston City Hospital and Massachusetts Memorial Hospitals. Of these only 7 (9 per cent) were operable. Overholt³³ found 26 per cent of his cases to be operable. It may therefore be assumed that somewhere between 10 and 25 per cent of cases are operable when first considered for surgery, a sad reflection on the ability of physicians to recognize this relatively frequent disease in its early and favorable stages.

The contraindications for pneumonectomy, which in most cases constitute the reasons for inoperability and as a corollary mean a late diagnosis and advanced disease, are based on certain findings. These have been summarized by Graham³⁴ as follows:

The presence of bloody pleural fluid. This usually means invasion of the visceral and parietal pleura by the growth. In most cases, the presence of clear effusions also means inoperability, and the finding of tumor cells in such effusions makes it certain.

Paralysis of the corresponding half of the diaphragm, as determined by fluoroscopic examination. This usually is evidence of invasion of the phrenic nerve.

Paralysis of the left vocal cord in cases of left-sided bronchogenic carcinoma. This usually denotes invasion of the left recurrent nerve as it passes under the arch of the aorta.

Severe pain in the thoracic wall or down the arm. This is a bad sign and generally is evidence of an involvement of intercostal nerves or of the brachial plexus. The presence of a moderate amount of pain, however, should not preclude an exploratory operation.

Bronchoscopic evidence of extension of the tumor into the trachea. This usually contraindicates pneumonectomy, although occasionally it is possible to remove even a part of the wall of the trachea.

The presence of distant metastases. In exceptional cases it may prove justifiable to remove both the lung and a solitary metastasis.

The question of the age of the patient is important from the standpoint of operability, but at least up to the present time there is no fixed limit. The general condition, and particularly that of the cardiovascular apparatus is more important than the chronological age. (Graham's oldest patient

to survive was sixty-eight; another patient of seventy years made an immediately satisfactory recovery but died suddenly of coronary thrombosis one week later.)

In view of the frequency of the occurrence of the disease and its insidious character in the early stages, only a concerted effort, together with the acquisition of a nation-wide state of awareness to bronchogenic cancer on the part of the medical profession as a whole, will result in early diagnosis for a greater number of patients afflicted with this disease and a consequent improvement of the chances for cure.

Any male patient of middle age or beyond who develops cough and expectoration, with or without hemoptysis or blood streaking, and who cannot be shown to have tubercle bacilli in the sputum should be considered to have bronchogenic carcinoma until it is proved unequivocally that there is some other reason for his symptoms.

The first step leading to diagnosis is, of course, a roentgenogram of the chest. In most cases this simple procedure suggests the diagnosis either by indirect evidence, such as atelectasis of a lobe or lobes due to an obstructive bronchial lesion, or by the more positive evidence of an infiltrative hilar lesion or parenchymal tumor. Alexander³⁵ states that despite the prevailing impression, most *circumscribed* intrathoracic neoplasms are intrapulmonary and malignant. All pulmonary abscesses and suppurative lesions should be considered as resulting from bronchogenic carcinoma. In general, one may say that the roentgenogram shows the tumor, which may be relatively tiny, less frequently than its result, which usually predominates in the clinical picture. In rare cases the roentgenogram is negative. In any event, the second step is almost always bronchoscopy, by which a positive diagnosis before operation can best be made. In Graham's³⁴ experience a positive diagnosis can be made by bronchoscopic biopsy in about 75 per cent of cases. Holinger and Radner³⁶ state that in Jackson's series a diagnosis by biopsy was possible in 75 per cent of cases of bronchial cancer, and that Kramer and Som obtained a positive tissue diagnosis in 74 per cent of cases and Clerf in 68 per cent.

The problem of what advice to give in the 25 per cent of cases without a positive diagnosis is an important one. In Graham's³⁴ opinion, the answer is generally fairly simple. If there is a reasonable suspicion of carcinoma, an exploratory thoracotomy should be performed without delay, for in this way many lives can be saved. Too often the advice of the physician has been to wait to see if anything happens. Nothing is gained by this delay, and the usual result is another victim.

An analysis of the risks involved in pneumonectomy reveals an encouraging trend for an operation that must be considered to be technically still in its

developmental stage. In 1940, seven years after the first successful pneumonectomy for bronchogenic cancer, Churchill³² reported hospital deaths in 14 (67 per cent) of 21 patients undergoing total pneumonectomy. Fifteen of the 27 patients subjected to resection — lobectomy and pneumonectomy — died in the hospital, and 7 died subsequently of their disease. At the time of the report, 5 of 155 patients with proved primary carcinoma were alive with no apparent residual or recurrent disease. Churchill finds these results to be similar to those reported by Edwards, who noted a salvage of 6 patients out of a total of 172 cases. In 1940, Samson and Holman³⁷ reported 5 cases with 4 recoveries, and in the same year, Ochsner and DeBakey³⁸ reported 19 cases with 10 recoveries. In 1941, Overholt³³ reported 31 cases with 9 operative deaths (29 per cent). Graham³⁴ reports that in the last 25 cases of pneumonectomy performed by him and Blades there were only 3 deaths, a mortality of 12 per cent.

Graham further discusses the question. Shall the thoracic surgeon offer a chance, even though a small one, to the bad-risk victim of bronchogenic carcinoma, or shall he decline to operate because of the great danger of an operative mortality? He believes that most thoracic surgeons offer the patient a chance of recovery. A mortality of 12 per cent in 25 cases is a respectable one, and should dispel the all too widespread belief that the operation of total pneumonectomy for primary cancer carries with it an enormous operative risk. It should be remembered that without operation the risk is 100 per cent.

BRONCHIECTASIS

It is now generally agreed that the definitive treatment of bronchiectasis is surgical, and that most patients in whom it is discovered should be considered for lobectomy or pneumonectomy, although many may, after evaluation, be denied operation for a variety of reasons.

Corroboration of this statement is obtained in several recent studies, one of the best of which is presented by Perry and King.³⁹ Basing their conclusions on a follow-up of 400 patients, these authors show that in a twelve-year study the mortality in the nonsurgically treated cases was 26 per cent, 41 per cent of these patients dying within five years of onset and 15 per cent living twenty years or longer after onset. Of the patients who died, 78 per cent died directly from their disease. Some statistical evidence supports the view that patients who develop bronchiectasis before the age of ten do not live beyond the age of forty. Thus, of persons with the onset in the first decade only 9 per cent were living at the age of forty or over. Of the 59 patients who reached the age of forty or over, in only 15 per cent was the onset in the first decade. The operative mortality in one hundred and twenty-two

modern-type lobectomies performed on 116 patients (by Churchill at the Massachusetts General Hospital) was 3 per cent. The working and living capacity of the traced living patients was considered to be excellent in 67 per cent of the surgical group and 38 per cent of the nonsurgical group. These authors find nonsurgical treatment to be only palliative and believe that because of the steadily decreasing operative mortality rate, simple lobectomy may be advised without hesitation. Even with bilateral disease the risk in bilateral lobectomy — of course in two stages — is often not too great.

Bradshaw, Putney and Clerf⁴⁰ studied 242 patients with bronchiectasis. Of these 112 were living and 59 died from bronchiectasis or its complications.

Riggins⁴¹ found the mortality for 85 patients with medically treated bronchiectasis collected during ten years with many observed for only three or four years, to be 14 per cent. He concludes, "The morbidity and mortality of untreated and medically treated bronchiectasis . . . is such that the physician who routinely advises young adults with operable bronchiectasis against surgery, is assuming a grave responsibility and in all probability renders his patient a great disservice." It should be added that children stand thoracic operations exceptionally well, and lobectomy early in life is almost certain to obviate the hazards of bronchiectasis that such children must face if they grow to adolescence or adult life with nonsurgical treatment.

Averaging the figures given by various students of the disease, Hinshaw and Schmidt⁴² estimate that less than 10 per cent of patients with severe bronchiectasis obtain a satisfactory result from any form of medical treatment, and conclude that the mortality rate within ten or fifteen years after the diagnosis is made is somewhere between 30 and 50 per cent. When severe bronchiectasis appears in childhood, it is improbable that the patient will live beyond the age of forty years.

The development of the modern technic⁷ of intrahilar dissection and individual ligation has further improved the operation of lobectomy as applied to bronchiectasis. Although occasionally not feasible or even impossible in cases of so-called "frozen hilus" owing to dense fibrosis resulting from repeated exacerbations of pneumonitis, this technic materially reduces the postoperative complications of empyema and bronchopleural fistula already alluded to in the section on lobectomy in tuberculosis. The advent and increasing availability of penicillin promises a further reduction in the incidence of postoperative empyema. At the Massachusetts Memorial and Boston City hospitals it has already been used prophylactically, in a few cases both intrapleurally and intramuscularly, as part of the postoperative routine, with gratifying results. It is still too soon, however, to draw any definite conclusions.

Additions to the knowledge of the surgical anatomy of the detailed structure of the lung, refinements in bronchography and clinical experience have demonstrated that a lobe of the lung is actually made up of a cluster of bronchopulmonary segments. In this connection an important contribution was made by Churchill and Belsey¹¹ in 1939. They correctly prophesied that the bronchopulmonary segment would replace the lobe as the surgical unit of the lung. Although it had been suggested by Nelson⁴³ in 1934 that the lungs are made up of eight lobes—two upper lobes, two middle lobes, the dorsal divisions of the lower lobes and the basal divisions of the lower lobes—it remained for these surgeons to demonstrate the actual clinical application of such an anatomic configuration. They applied the principle of segmental pneumonectomy to resection of the lingula of the left upper lobe—left middle lobe—by removing the posteromedial segment of the lingula, and also employed the technic in operations on the dorsal divisions of the lower lobes. In a recent paper, Blades⁴⁴ describes a technic for other partial excisions, for example, of the basal division of the lower lobe. He used it satisfactorily in 8 cases, with no deaths. Such contributions are of value since they point the way to greater conservation of normal pulmonary tissue in certain lesions well localized in a bronchovascular segment of the lung.

No discussion of the operative treatment of a disease is complete without reference to the risks involved. Churchill's excellent figures, as reported by Perry and King,³⁹ have been mentioned. Bradshaw and O'Neill⁴⁵ report the results of surgical treatment of bronchiectasis in 76 patients whose disorder was mostly due to an unknown etiologic agent. One death occurred among the 24 patients with disease of the lower lobe and of the lower lobe and lingula, a mortality of 4 per cent. Among 26 patients in whom one lobe was removed but disease was present in other lobes there were 4 deaths, a mortality of 15 per cent. Seventeen patients had two or more lobes removed, with 3 deaths, a mortality of 18 per cent; 11 had disease in other lobes. Maier⁴⁶ reports 64 cases in which pulmonary resections for bronchiectasis were performed. Lobectomy was done in 55 cases, and pneumonectomy in 9, with 1 operative death, a mortality of less than 2 per cent.

Bilateral lobectomy, in stages, has frequently been performed for bronchiectasis. It is now considered routinely in planning the surgical program of suitable bilateral cases. Churchill³² reports 6 cases with 1 death. We have performed bilateral excision in 4 cases with no death. As might be expected, however, and, as is borne out in Bradshaw and O'Neill's⁴⁵ figures, bilateral lobectomy is associated with considerably higher mortality, since it subjects the patient to two major operations.

Moreover, the postoperative period after the first lobectomy is rendered more hazardous because the patient must convalesce with disease remaining in one or more lobes.

PSEUDOBRONCHIECTASIS

In a communication emphasizing the importance of the effects of atypical pneumonia on the bronchi and the production of pseudobronchiectasis, Blades and Dugan⁴⁷ state that 6 patients with almost identical histories have been observed at the Walter Reed Hospital. Bronchograms, following an acute illness diagnosed as atypical pneumonia, demonstrated bronchial dilatations, but after a period of one or two months the configuration of the bronchi returned to normal. The authors therefore believe that atypical pneumonia can produce temporary enlargement of the bronchi, and urge that surgical intervention be delayed in questionable cases until repeated bronchograms and the clinical features of the disease establish an unequivocal diagnosis of anatomic bronchiectasis.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30361

PRESENTATION OF CASE

First admission. A fifty-nine-year-old mechanic was admitted to the hospital because of swelling of the legs and ankles.

The patient had been in excellent health until four months before entry, when he noticed swelling of the ankles and legs, especially at the end of the day. Soon after, he developed exertional dyspnea. He had apparently slept on two pillows all his life and continued to do so without any change. The swelling, however, increased and progressed to involve the scrotum and penis. About two months before entry he gave up his job and was hospitalized in a community hospital for one week. There he was given three pills daily and numerous injections; the nature of these was not known. The swelling of the legs subsided; he felt much better and was discharged to the care of his physician, who continued to give him two injections a week and three capsules daily. Following discharge, however, his symptoms gradually returned. He had had no orthopnea, paroxysmal nocturnal dyspnea, chest pain or palpitation. Edema of the ankles and legs and exertional dyspnea, however, progressed, and the abdomen became slightly larger. His appetite had remained essentially the same.

The past history was negative.

*On leave of absence

Physical examination showed a well-developed, well-nourished man in no discomfort. The left border of cardiac dullness was 4 cm. to the left of the midclavicular line. The rate was slow (48) but regular except for an extrasystole every tenth or fifteenth beat, with compensatory pauses. A loud systolic murmur was heard over the whole precordium but was maximal over the aortic area, accompanied by a questionable systolic thrill. The murmur was well transmitted up the neck vessels. There was a questionable early diastolic murmur to the left of the sternal border. The pulmonic second sound was greater than the aortic. Crackling rales were heard at both bases. The liver edge was palpable two fingerbreadths below the costal margin. Massive pitting peripheral edema, as well as edema of the penis, scrotum and sacrum, was present.

The blood pressure was 145 systolic, 70 diastolic. The temperature was 98.6°F., the pulse 48, and the respirations 22.

Examination of the blood showed a red-cell count of 4,100,000, with 13.4 gm. of hemoglobin. The white-cell count was 9000, with 67 per cent neutrophils. The urine gave a ++ test for albumin but was otherwise negative. A Wassermann and two Hinton tests were negative.

The patient was given 4 cc. of Cedilanid and 2.2 cc. of Mercupurin. One half hour later the radial pulse was 27, but he had no subjective symptoms. An electrocardiogram on the following day showed auricular fibrillation with an average rate of 42. The ST₁ and ST₂ waves were depressed, the T₁ and T₂ waves diphasic, and the T₃ waves low. T was inverted in CF₁. The nonprotein nitrogen was 39.5 mg. per 100 cc.

The patient was given 3 gm. (45 gr.) of ammonium chloride daily. An electrocardiogram one day after the first tracing revealed no significant change. On the fourth hospital day he was started on 0.1 gm. (1½ gr.) of digitalis daily and was given 2.2 cc. of Mercupurin intravenously which was repeated two days later. He continued to receive ammonium chloride and digitalis daily and re-

sponded well. On the tenth hospital day examination of the heart revealed slow fibrillation. The sounds were of good quality. There was no deficit. There were dry rales in the lung bases and sticky prolongation of the breath sounds. The edema had cleared except in the left calf, where it was apparently due to marked superficial and deep varicosities. The right calf was relatively unaffected. An x-ray film of the chest on the following day showed gross enlargement of the heart, both to the right and to the left. The transverse diameter of the heart was 19.5 cm., with an internal chest diameter of 34.0 cm. The lung fields were clear. There was no fluid in the costophrenic sinuses.

On the twelfth hospital day, the lungs were clear to auscultation and the patient had no orthopnea or dyspnea. There was no edema except for slight swelling of the left leg. He was discharged home on 0.1 gm. of digitalis and 3 gm. of ammonium chloride daily and a low-salt and low-fluid diet and was advised to remain inactive.

Final admission (seventeen days later). Following discharge the patient did well for one week. At the end of that period he contracted a cold, with rapid recurrence of the previous symptoms of dyspnea and edema. He then experienced increasing orthopnea. His condition progressed rapidly so that in about five days edema had reached the sacrum, involving both legs, the scrotum and the penis. Two weeks after discharge he returned to the Out Patient Department, where the intravenous injection of Mercupurin gave no relief. He was admitted two days later.

Physical examination showed an extremely dyspneic and orthopneic man with an unproductive cough. The heart was slowly fibrillating, with a rate of 60 and without any pulse deficit. The heart was otherwise the same as before. There was fluid in both lung bases, and basal moist rales. The liver edge was palpated seven fingerbreadths below the costal margin. Ascites was present as well as a marked pitting edema of the extremities up to the sacrum.

The blood pressure was 158 systolic, 88 diastolic. The temperature was 96°F., the pulse 70, and the respirations 20.

Examination of the blood showed a red-cell count of 5,020,000, with 11.5 gm. of hemoglobin. The white-cell count was 9200, with 70 per cent neutrophils.

The patient was given intravenous Mercupurin and oral digitalis and ammonium chloride. On the second hospital day he was found to be unable to void; he was catheterized, at which time only 45 cc. of urine could be obtained. This showed a ++ test for albumin, contained white cells and had a pH of 7. He was given 100 cc. of 50 per cent dextrose solution intravenously, followed by 100 cc. of physiologic saline solution, with little, if any, success. He had a great deal of respiratory

distress and became slightly cyanotic. The radial pulse rose to 90. The nonprotein nitrogen rose to 203 mg. per 100 cc. He died on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. C. SIDNEY BURWELL*: I should like to begin by commenting on the electrocardiogram and by seeing the x-ray films.

DR. BENJAMIN CASTLEMAN: Would you care to see the electrocardiogram?

DR. BURWELL: The fourth lead shows a strikingly inverted T wave. There is an upward wave that I should call an R, and a deep S. The ST₁ and ST₂ waves are depressed, but only slightly so. Fibrillary waves are perfectly apparent. The rate is slow, and it appears to be quite regular. I should place it as a regular rate originating in the ventricles.

In this x-ray film the left border of the heart is not straight, but it is a rather expressionless left border. In the oblique view was the right auricle enlarged?

DR. LAURENCE L. ROBBINS: I do not believe that one can tell, but I presume that the patient was fluoroscoped and that the notation in the record was made from that. In this lateral view it is rather hard to tell whether or not the auricle is enlarged.

DR. BURWELL: It is a big lobular heart in both directions, with enlargement of most of the chambers. Certainly the left ventricle is enlarged, and I suspect that the auricles are dilated.

I find this a complex and difficult case. I should like to discuss briefly three possibilities with regard to the nature of the disease. The first decision I should like to make is whether this patient had heart failure or some other cause for this progressive and recurrent edema and dyspnea, which eventually "did him in." There are several other possibilities. First, one raises the question of whether he had obstruction of the entry of blood into the heart which was on a mechanical obstructive basis rather than because of what we call heart failure. In other words, Did he have constrictive pericarditis or pericardial effusion? I believe that the evidence is strongly against both of them. The cardiac signs did not resemble those commonly observed in either of those situations, and I am content to set that diagnosis aside.

One asks, Did he have mechanical obstruction lower down in the venous system than the right auricle? The point has been made, and with a good deal of force, that the edema started at the feet and rose to the level of the sacrum and no higher. One wonders if that is a suggestion that he had a bilateral obstruction to returning venous circulation from his legs, perhaps on the basis of recurrent thrombosis extending up into the iliac

*Research professor of clinical medicine and dean, Harvard Medical School.

system and so on, or perhaps even into the inferior vena cava. He showed no evidence of collateral circulation, which he should have if he had had obstruction to the vena cava for some time. He had a few varicose veins in one leg that seem adequately to account for the extra edema on that side, but I should hesitate to blame the edema on venous obstruction. I am always impressed by the small amount of edema that is brought about by most venous obstruction.

One then asks, Did he have cirrhosis of the liver? To ask the question is to answer it in the negative. I believe. The same can be said of nephritis.

I am reasonably satisfied to conclude that the first item in this patient's diagnoses is heart failure, and I am comforted in that conclusion by the fact that he had certain findings that ordinarily go with congestive heart failure. He had a large heart, for example, and evidence of various kinds of cardiac disease. I shall accept heart failure as the first diagnosis.

The second decision concerns the nature of his cardiac disease, and here I find the going a good deal stormier. In the first place, the evidence is not altogether conclusive. If one sees a man of this age with a large heart, which this man certainly had, with a loud systolic murmur (I think this was loud for two reasons: the record says it was, and it was heard in the vessels of the neck) accompanied by a thrill and a diastolic murmur, one can be reasonably well advised to conclude that he has aortic stenosis. Aortic stenosis is no rare disorder. It is particularly common in men of this age. It is compatible with many years of continued good health and also compatible with a short and progressive period of cardiac failure leading to death from cardiac failure. One's confidence, however, in that diagnosis is rudely shaken by the word "questionable," which is attached to the most important sign. The best evidence of aortic stenosis is an unquestioned aortic thrill. Another almost incontrovertible evidence is the demonstration of calcium in the aortic valve. I cannot see calcium, but it usually is not seen in the film. Was it seen on fluoroscopy?

DR. ROBBINS: I doubt it.

DR. BURWELL: Is there any note to that effect?

DR. CASTLEMAN: No.

DR. BURWELL: So we do not have incontrovertible evidence of calcium or the definite evidence of a thrill. My impression of aortic stenosis is further shaken by the question mark put after the diastolic murmur. It is always comforting to have an aortic diastolic murmur. Most people with loud diastolic murmurs have heart disease, and even a higher percentage of people with diastolic murmurs have heart disease. Most people with early diastolic murmurs at the left sternal border have aortic regurgitation. If a man has

aortic regurgitation he almost always has disease of the aortic valve. The diagnosis of aortic stenosis is often made on the demonstration of aortic insufficiency. This man's blood pressure is quite compatible with aortic stenosis and regurgitation. He apparently did not have a greatly elevated peripheral blood pressure, but he did have a wide pulse, which tends to support the existence of this questionable diastolic murmur. On the other hand, one cannot lean too heavily on that for several reasons. In the first place, diastolic pressures are often variable or misleading. In the second place, a person with a slow pulse rate usually has a relatively wide pulse pressure for obvious reasons; it is a long time between systoles and the diastolic pressure has that much more time to fall. So I find myself in grave uncertainty whether or not this man had an aortic regurgitation, but it does appear that he had aortic stenosis. I shall come back to that in a moment.

I think that it is unnecessary to elaborate the point that he did not have syphilitic aortitis. Most people who develop heart failure on the basis of syphilitic aortitis have free aortic regurgitation. A few people who have syphilitic involvement of the coronary orifices develop heart failure on the basis of the coronary closure, and a very few people, usually young men, develop heart failure on the basis of syphilitic myocarditis. I see no reason to inject any of these possibilities.

I do not believe that he had a congenital form of heart disease. I do not see any evidence in the auscultation or by x-ray that would permit me to judge that. No statement is made about cyanosis except that he became cyanotic in the last days of his life, so I think we can assume that he was not cyanotic before that day.

Now we come to the electrocardiogram. An alternative or possibly an addition to the diagnosis of aortic stenosis is the diagnosis of diffuse myocardial disease due to repeated coronary occlusions. I say "repeated" because there is no mention in the history of any attacks of sufficient magnitude to have given him symptoms, and because he had the small complexes and the relatively flat T waves that one often sees with rather diffuse myocardial disease. Aortic stenosis is usually accompanied by a normal sinus rhythm if it is the only valvular lesion present. When one sees a patient with aortic stenosis who has auricular fibrillation, he looks eagerly for evidence of mitral stenosis in addition. This does not appeal to me as an ideally mitral-shaped heart. There is not the slightest suggestion of even a questionable mitral murmur. There is one other point in favor of coronary disease and that is that he certainly had a high degree of auriculoventricular block. He had a complete block at the time the electrocardiogram was taken, and usually the heart rate is below 50. Coronary disease

is certainly the commonest cause of auriculoventricular block. *Digitalis* presumably accounted for a certain degree of the block.

I am inclined to conclude, on the basis of somewhat uncertain signs, that this patient had as his primary variety of heart disease an aortic stenosis. I think there is no reason to doubt that he also had a diffuse myocarditis, even though the Q wave was upright.

The third question I should like to commit myself on is the nature of the terminal anuria. I can think of three or four vascular mechanisms that give an anuria. An aortic dissecting aneurysm with compression of the renal arteries has been known to produce anuria, but there is no reason to suspect that this man had a dissecting aneurysm. The second one has certain attractions, although the thought is rather far afield, that is, a thrombosis of the *vena cava* with occlusion of the renal veins. There have been a number of cases reported. It is rare but not impossible. It is almost always accompanied either by a great deal more evidence of venous thrombosis in the legs or by obvious collateral circulation around the groins, or both. The third is an embolic occlusion of the renal arteries or a sufficiently sizable number of infarcts in both kidneys so that anuria results. It is much likelier to come about from the type of embolus that originates in the fibrillating auricle than it is from acute or subacute endocarditis. On the whole I should be inclined to think, although I find no evidence of any other embolic incidents anywhere in the body, that this anuria was due to an acute interference with renal circulation on the basis of embolism. It may be that for a brief period this patient's fibrillation ceased, to be replaced by a normal rhythm, which is one of the ideal situations for multiple embolism and may have been the thing that explains this picture. Whenever one sees a man of fifty-nine who has progressive edema without previous evidence of cardiac failure, one is reminded that there is a type of tuberculosis of the pericardium that is particularly common in old men.

Because he was a fifty-nine-year-old man who had a large heart, a very rapidly progressive affair, with no fever, no x-ray evidence and no physical signs, I shall rest the case on four diagnoses: heart failure, aortic stenosis, diffuse myocardial disease associated with coronary arterial disease, and infarction of the kidney.

DR. CHESTER M. JONES: Is it not curious that the edema was from the abdomen down, so to speak, and that he had no engorged neck veins and other signs of right-sided failure, and no left-sided failure, as evidenced by orthopnea and dyspnea, until the terminal event?

DR. BURWELL: Those are all "curious incidents" as Sherlock Holmes would have said. Some can be rationalized. As a matter of fact, exertional dyspnea was almost as early a symptom as slight swelling

of the ankles. Exertional dyspnea presumably meant that he had a slight amount of pulmonary congestion. It is possible, although I do not know and I cannot tell from the x-ray film, that he was somewhat emphysematous. There is no statement to that effect. He ended up by having orthopnea. That is one of the reasons I am inclined to think that coronary heart disease was important. I believe that the right heart must have broken down with a relatively small amount of elevation of pulmonary pressure.

A PHYSICIAN: Was there a fall in blood pressure?

DR. CASTLEMAN: It was never very high, being 155 systolic when he came in. Just before he died it was 145 systolic, 65 diastolic. It stayed about the same throughout.

CLINICAL DIAGNOSES

Arteriosclerotic heart disease, with congestive failure.

Renal failure and uremia (?cause).

DR. BURWELL'S DIAGNOSES

Congestive heart failure.

Aortic stenosis.

Myocardial disease, based on coronary-artery disease.

Infarction of kidney.

ANATOMICAL DIAGNOSES

Endocarditis, chronic, rheumatic, with moderate aortic and mitral stenosis and slight tricuspid stenosis.

Coronary sclerosis.

Myocardial fibrosis.

Acute glomerulonephritis.

Endocarditis, acute, terminal: mitral and aortic.

Pericarditis, acute and chronic.

Congestive cardiac failure.

Congestion of liver.

Ascites.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: On the four counts that Dr. Burwell mentioned, he was correct on three. This man had heart failure. At the time of autopsy, ascites and severe chronic passive congestion of the liver were found. The heart was quite large, weighing 600 gm. He had aortic stenosis of the calcareous type, but it was mild as compared with some that we have seen. He also had a moderate degree of mitral stenosis, with thickening of the chordae tendineae, and in addition, slight involvement of the tricuspid valve; so that there is no question that he had rheumatic heart disease. There were superimposed on the mitral and aortic valves tiny

vegetations, which were merely evidence of an acute terminal endocarditis. The coronary arteries were markedly sclerotic, being narrowed in some places to pinpoint lumens. Throughout the myocardium there were small areas of fibrosis, but nothing at all recent.

The kidneys were very striking. They weighed over 600 gm., about twice the normal size, and were markedly swollen, with numerous red depressed areas scattered throughout. Microscopic examination showed old vascular disease, which accounted for the depressed areas. Every glomerular tuft was markedly swollen and filled with polymorphonuclears—findings characteristic of an acute glomerulonephritis and undoubtedly the cause of the anuria. Most of the glomeruli contained 40 to 50 polymorphonuclear cells. The tubules were swollen but contained no red cells.

DR. BURWELL: I ought to say why I ruled out tricuspid stenosis. The major reason was that he was so well up to the time he developed failure. Most people with serious tricuspid stenosis have had venous congestion of the liver for a long time. Since this patient did not have a chronically enlarged liver, I laid that diagnosis aside.

DR. CASTLEMAN: The stenosis of the mitral valve was not marked, and the tricuspid disease, although definite, was only slight. He had a pericarditis that was both old and recent.

CASE 30362

PRESENTATION OF CASE

First admission. A sixty-year-old housewife entered the hospital because of intestinal obstruction.

Twenty-two years before entry the patient had an appendectomy, and ten years later an operation for fibroids of the uterus. Since that time she had had repeated attacks of abdominal pain, tenderness and distention, relieved by medication prescribed by her family physician. For the two years preceding entry, whenever the stools were formed, they were ribbon-like; otherwise they consisted of watery fluid. On two occasions she had passed bright-red blood. Seven weeks before entry she had a severe attack of abdominal pain and was completely obstructed and distended for three days; she was relieved for three days but again became obstructed and distended for three days. At that time she first noticed a tender stationary lump in the left side of the abdomen. She had lost about 15 pounds.

Physical examination showed a well-developed pale woman with evidence of recent weight loss. The abdomen was protuberant. In the left mid-abdomen was a hard mass the size of a golf ball, which was extremely tender and slightly movable. No other organs or masses were palpable.

The blood pressure was 140 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,210,000, with 65 per cent hemoglobin. A white-cell count was 12,500, with 76 per cent neutrophils. The urine was normal. The stools were guaiac negative. Plain x-ray films of the abdomen showed the proximal half of the colon to be dilated and filled with feces and a small quantity of gas extending slightly to the left of the midtransverse colon.

On the third hospital day an exploratory laparotomy revealed a colloid adenocarcinoma of the splenic flexure. A Mikulicz resection was performed. The distal loop of the bowel was sutured to the lateral abdominal wall to prevent the small bowel from getting into the denuded area.

The patient did well for about twelve days, but subsequently began to have attacks of lower abdominal cramps associated with profuse bowel movements. The abdomen became distended during these attacks. In the course of the next month and a half, however, these disappeared; a clamp was then applied to the stoma, and a good spur cut through. She was discharged on the sixtieth post-operative day to return in two months for closure of the colostomy.

Second admission (three months later). After discharge the patient felt well and gained 12 to 15 pounds. The colostomy had worked well until recently, when she noticed a little bright-red blood mixed with the stools and a little bleeding from the colostomy opening.

Physical examination was essentially negative.

On the fifth hospital day the colostomy was closed. Postoperatively she was bothered by impacted feces in the rectum and, when relieved of this, developed diarrhea with abdominal cramps of the type that she had had for years. Subsequently, however, the bowel movements became normal and she was discharged on the eleventh postoperative day.

Third admission (twenty-seven months later). Following discharge the patient did well for some time but presumably had further symptoms of obstruction and was operated on in a community hospital for lysis of adhesions. She was then apparently well until ten or twelve days before re-entry, when she developed severe abdominal cramps and became distended. She was taken to the same outside hospital, where an ileostomy was performed. She developed a fecal fistula in the wound, the cramps persisted, and she was transferred to this hospital.

Physical examination showed tenderness in the abdomen, which was not greatly distended. A small rubber tube protruded from the left side at the level of the umbilicus. There was a fecal fistula to the right of and inferior to the umbilicus, with considerable porky induration about the fistula

is certainly the commonest cause of auriculoventricular block. Digitalis presumably accounted for a certain degree of the block.

I am inclined to conclude, on the basis of somewhat uncertain signs, that this patient had as his primary variety of heart disease an aortic stenosis. I think there is no reason to doubt that he also had a diffuse myocarditis, even though the Q wave was upright.

The third question I should like to commit myself on is the nature of the terminal anuria. I can think of three or four vascular mechanisms that give an anuria. An aortic dissecting aneurysm with compression of the renal arteries has been known to produce anuria, but there is no reason to suspect that this man had a dissecting aneurysm. The second one has certain attractions, although the thought is rather far afield, that is, a thrombosis of the vena cava with occlusion of the renal veins. There have been a number of cases reported. It is rare but not impossible. It is almost always accompanied either by a great deal more evidence of venous thrombosis in the legs or by obvious collateral circulation around the groins, or both. The third is an embolic occlusion of the renal arteries or a sufficiently sizable number of infarcts in both kidneys so that anuria results. It is much likelier to come about from the type of embolus that originates in the fibrillating auricle than it is from acute or subacute endocarditis. On the whole I should be inclined to think, although I find no evidence of any other embolic incidents anywhere in the body, that this anuria was due to an acute interference with renal circulation on the basis of embolism. It may be that for a brief period this patient's fibrillation ceased, to be replaced by a normal rhythm, which is one of the ideal situations for multiple embolism and may have been the thing that explains this picture. Whenever one sees a man of fifty-nine who has progressive edema without previous evidence of cardiac failure, one is reminded that there is a type of tuberculosis of the pericardium that is particularly common in old men.

Because he was a fifty-nine-year-old man who had a large heart, a very rapidly progressive affair, with no fever, no x-ray evidence and no physical signs, I shall rest the case on four diagnoses: heart failure, aortic stenosis, diffuse myocardial disease associated with coronary arterial disease, and infarction of the kidney.

DR. CHESTER M. JONES: Is it not curious that the edema was from the abdomen down, so to speak, and that he had no engorged neck veins and other signs of right-sided failure, and no left-sided failure, as evidenced by orthopnea and dyspnea, until the terminal event?

DR. BURWELL: Those are all "curious incidents" as Sherlock Holmes would have said. Some can be rationalized. As a matter of fact, exertional dyspnea was almost as early a symptom as slight swelling

of the ankles. Exertional dyspnea presumably meant that he had a slight amount of pulmonary congestion. It is possible, although I do not know and I cannot tell from the x-ray film, that he was somewhat emphysematous. There is no statement to that effect. He ended up by having orthopnea. That is one of the reasons I am inclined to think that coronary heart disease was important. I believe that the right heart must have broken down with a relatively small amount of elevation of pulmonary pressure.

A PHYSICIAN: Was there a fall in blood pressure?

DR. CASTLEMAN: It was never very high, being 155 systolic when he came in. Just before he died it was 145 systolic, 65 diastolic. It stayed about the same throughout.

CLINICAL DIAGNOSES

Arteriosclerotic heart disease, with congestive failure.

Renal failure and uremia (?cause).

DR. BURWELL'S DIAGNOSES

Congestive heart failure.

Aortic stenosis.

Myocardial disease, based on coronary-artery disease.

Infarction of kidney.

ANATOMICAL DIAGNOSES

Endocarditis, chronic, rheumatic, with moderate aortic and mitral stenosis and slight tricuspid stenosis.

Coronary sclerosis.

Myocardial fibrosis.

Acute glomerulonephritis.

Endocarditis, acute, terminal: mitral and aortic.

Pericarditis, acute and chronic.

Congestive cardiac failure.

Congestion of liver.

Ascites.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: On the four counts that Dr. Burwell mentioned, he was correct on three. This man had heart failure. At the time of autopsy, ascites and severe chronic passive congestion of the liver were found. The heart was quite large, weighing 600 gm. He had aortic stenosis of the calcareous type, but it was mild as compared with some that we have seen. He also had a moderate degree of mitral stenosis, with thickening of the chordae tendineae, and in addition, slight involvement of the tricuspid valve; so that there is no question that he had *rheumatic heart disease*. There were superimposed on the mitral and aortic valves tiny

vegetations, which were merely evidence of an acute terminal endocarditis. The coronary arteries were markedly sclerotic, being narrowed in some places to pinpoint lumens. Throughout the myocardium there were small areas of fibrosis, but nothing at all recent.

The kidneys were very striking. They weighed over 600 gm., about twice the normal size, and were markedly swollen, with numerous red depressed areas scattered throughout. Microscopic examination showed old vascular disease, which accounted for the depressed areas. Every glomerular tuft was markedly swollen and filled with polymorphonuclears—findings characteristic of an acute glomerulonephritis and undoubtedly the cause of the anuria. Most of the glomeruli contained 40 to 50 polymorphonuclear cells. The tubules were swollen but contained no red cells.

DR. BURWELL: I ought to say why I ruled out tricuspid stenosis. The major reason was that he was so well up to the time he developed failure. Most people with serious tricuspid stenosis have had venous congestion of the liver for a long time. Since this patient did not have a chronically enlarged liver, I laid that diagnosis aside.

DR. CASTLEMAN: The stenosis of the mitral valve was not marked, and the tricuspid disease, although definite, was only slight. He had a pericarditis that was both old and recent.

CASE 30362

PRESENTATION OF CASE

First admission. A sixty-year-old housewife entered the hospital because of intestinal obstruction.

Twenty-two years before entry the patient had an appendectomy, and ten years later an operation for fibroids of the uterus. Since that time she had had repeated attacks of abdominal pain, tenderness and distention, relieved by medication prescribed by her family physician. For the two years preceding entry, whenever the stools were formed, they were ribbon-like; otherwise they consisted of watery fluid. On two occasions she had passed bright-red blood. Seven weeks before entry she had a severe attack of abdominal pain and was completely obstructed and distended for three days; she was relieved for three days but again became obstructed and distended for three days. At that time she first noticed a tender stationary lump in the left side of the abdomen. She had lost about 15 pounds.

Physical examination showed a well-developed pale woman with evidence of recent weight loss. The abdomen was protuberant. In the left mid-abdomen was a hard mass the size of a golf ball, which was extremely tender and slightly movable. No other organs or masses were palpable.

The blood pressure was 140 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,210,000, with 65 per cent hemoglobin. A white-cell count was 12,500, with 76 per cent neutrophils. The urine was normal. The stools were guaiac negative. Plain x-ray films of the abdomen showed the proximal half of the colon to be dilated and filled with feces and a small quantity of gas extending slightly to the left of the midtransverse colon.

On the third hospital day an exploratory laparotomy revealed a colloid adenocarcinoma of the splenic flexure. A Mikulicz resection was performed. The distal loop of the bowel was sutured to the lateral abdominal wall to prevent the small bowel from getting into the denuded area.

The patient did well for about twelve days, but subsequently began to have attacks of lower abdominal cramps associated with profuse bowel movements. The abdomen became distended during these attacks. In the course of the next month and a half, however, these disappeared; a clamp was then applied to the stoma, and a good spur cut through. She was discharged on the sixtieth post-operative day to return in two months for closure of the colostomy.

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On the fifth hospital day the colostomy was closed. Postoperatively she was bothered by impacted feces in the rectum and, when relieved of this, developed diarrhea with abdominal cramps of the type that she had had for years. Subsequently, however, the bowel movements became normal and she was discharged on the eleventh postoperative day.

Third admission (twenty-seven months later). Following discharge the patient did well for some time but presumably had further symptoms of obstruction and was operated on in a community hospital for lysis of adhesions. She was then apparently well until ten or twelve days before re-entry, when she developed severe abdominal cramps and became distended. She was taken to the same outside hospital, where an ileostomy was performed. She developed a fecal fistula in the wound, the cramps persisted, and she was transferred to this hospital.

Physical examination showed tenderness in the abdomen, which was not greatly distended. A small rubber tube protruded from the left side at the level of the umbilicus. There was a fecal fistula to the right of and inferior to the umbilicus, with considerable porky induration about the fistula

and over the central part of the abdomen, associated with cramps. When the abdomen tightened, it bulged, peristalsis increased, and then gas and feces extruded.

Examination of the blood showed a white-cell count of 10,400, with 75 per cent neutrophils. The serum chloride was 87 milliequiv. per liter, and the protein 5.1 gm. per 100 cc.

The patient was given a transfusion, and an enterostomy was performed. Postoperatively there was some relief, but she continued to have attacks of abdominal cramps. On the sixteenth day she had a spontaneous bowel movement by rectum. She gradually improved. The enterostomy tube was clamped and taken out. Drainage stopped, and she was discharged on the forty-third hospital day.

Fourth admission (six years later). Following discharge the patient did well until one year before re-entry, when she noted that the stools were covered with blood. Ten days before admission she became obstructed, with marked distention. Four days later she had a bout of severe abdominal pain, followed two days later by the passage of small amounts of blood with the stools on three or four occasions. Two days before entry she had a massive hemorrhage and apparently went into shock, since she awoke lying on the bathroom floor without any recollection of falling, but with bruises on the face and head. She was brought into the hospital shortly thereafter. No additional information was available.

Physical examination showed a pale, thin woman in no distress. There was considerable evidence of weight loss. The heart and lungs were normal. A small sausage-shaped nontender mass was palpable immediately above the umbilicus.

The blood pressure was 140 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a hemoglobin of 9.1 gm., and a white-cell count of 7400, with 82 per cent neutrophils. The urine showed a + test for albumin. The stools were tarry and liquid, with a +++ guaiac test. The nonprotein nitrogen was 25 mg. per 100 cc., and the serum protein 5.8 gm. Barium examination of the colon showed an area of narrowing toward the lower end of the descending colon, which fluoroscopically was thought to be due to spasm but on the films was suggestive of an annular filling defect. No obstruction to the free flow of barium was encountered. In the midtransverse colon was an annular defect measuring 8 cm. in length, with an irregular lumen and shelf formation at either end. This defect was constant and coincided with the sausage-shaped mass in the abdomen. The right colon filled normally. A postevacuation film showed complete contraction of the colon and that most of the barium had been expelled; the filling defect in the transverse colon showed no change in its configura-

tion, and the appearance of the narrowing at the lower end of the descending colon was less conclusive.

The patient was given several transfusions, and on the seventeenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. IRA T. NATHANSON: The findings in this patient at the time of the last admission are those of a lesion of the colon. Questions arise whether the lesion was benign or malignant and whether it was related to the previous illness.

One may first consider the possibilities of a benign lesion. Chronic granulomas, such as tuberculosis and syphilis, may occur in the colon. Tuberculosis may exist in the colon as a localized process either in the hyperplastic or ulcerative form. In a fairly high percentage of cases, however, it is an accompaniment of the disease elsewhere and is usually confined to the cecum and ascending colon. The localized type of disease may produce obstruction and involve the bowel in an annular fashion when deep ulceration occurs. A mass may sometimes be palpated, but massive bleeding is rare, although it may occur in the ulcerative type. The apparent absence of extracolonic tuberculosis, the location of the lesion, the massive bleeding and the past history seem to rule out tuberculosis. Syphilis is certainly a rare entity especially without other evidence and, like sarcoid, which is said to occur in the large bowel, can be dismissed.

Chronic diverticulitis is a remote possibility. In general, the process is diffuse, and in well over half the cases it involves the sigmoid. When other parts of the colon are affected it is unusual not to have coincident lesions in the sigmoid. The symptoms prior to and soon after the resection of the splenic flexure may have been caused by diverticulitis, since carcinoma and diverticulitis may co-exist. I should, however, expect better x-ray evidence, as well as other signs and symptoms between the third and fourth admissions. Finally, bleeding is a relatively rare symptom in diverticulitis.

Segmental ulcerative colitis may also be mentioned. As a rule it appears in young people, the symptoms are profound, and it almost always involves the rectum and sigmoid colon. X-ray examination usually reveals characteristic signs, particularly evidence of inflammation of the mucosa, in addition to a defect. Furthermore, proctoscopic examination usually yields significant information.

Of the benign tumors, which include many varieties, adenomas or polyps deserve the only consideration. These are frequently multiple and occur with greatest frequency in the left half of the colon, particularly the lower portion. Occasionally, they are of sufficient size to produce obstructive symptoms and may ulcerate and bleed. They seldom

become large enough to be palpated on abdominal examination and are rarely, if ever, capable of producing the picture of an annular defect by x-ray examination. Intussusception, which is usually due to a polyp that has ulcerated and bled, may mimic the present picture; however, shelf formation, as seen by x-ray examination, is apparent at only one end.

Finally, we arrive at the most likely diagnosis. The symptoms, physical signs, laboratory evidence and x-ray findings are compatible with a malignant neoplasm of the colon. The decision must be made whether this was a carcinoma or one of the rarer lesions, such as a malignant lymphoma, a malignant carcinoid or even a malignant melanoma. Malignant lymphoma arises most frequently in the region of the cecum and from the submucosal lymphoid tissue of the bowel wall. It follows the cleavage planes and therefore may grow to a considerable size before obstruction, annular constriction and ulceration with hemorrhage appear. The other lesions are only of academic interest.

It therefore seems apparent that the syndrome was produced by carcinoma. Two questions arise that must be answered. Was this a new or recurrent tumor? Was it a single or a double lesion? The disease may have represented an extension of the previous carcinoma of the splenic flexure. Processes were described in the midtransverse colon and in the lower end of the descending colon. Each of these is a considerable distance from the first carcinoma, and from the x-ray report one may assume an area of normal bowel in the region of the bowel resection, which was between the two lesions described. Moreover, it is very unusual to find a recurrence of a cancer of the colon after a five-year interval of freedom from disease. According to the history, the final symptoms appeared about seven and a half years after the first admission. Hence, there seems to be little doubt that the original lesion was cured. It is well recognized that multiple primary cancers of the colon may occur simultaneously or successively over a period of years. When two or more cancers occur simultaneously they frequently arise in pre-existing polyps. Successive malignant changes in polyps, however, are also possible. In this case such a situation may have occurred. Thus it is problematical whether this was a single or a double lesion and whether the origin was in a polyp. The absence of polyps by x-ray examination, even though they are occasionally difficult to demonstrate, and the variability of the findings in the descending colon suggest a single primary cancer of the transverse colon. Such a lesion can arise in a polyp, and if one accepts the presence of a second cancer in the descending colon, then origin from a polyp is likely.

The x-ray defect in the lower colon seems to have been due to spasm, which often occurs, especially after a bowel resection.

If one ventures a guess concerning the type of such a neoplasm, it should be based on the location of the lesion, the form most frequently seen at that site, and the history. Cancer of the transverse colon is usually of the scirrhus type, which produces annular constriction of the colon. It may remain localized for a relatively long period of time and thus may attain considerable size before producing severe symptoms. The type of lesion seen oftenest is an adenocarcinoma, particularly if it arises on the basis of a polyp. In general they are of low to moderate malignancy.

CLINICAL DIAGNOSIS

Carcinoma of transverse colon.

DR. NATHANSON'S DIAGNOSIS

Primary adenocarcinoma of transverse colon (moderate malignancy).

ANATOMICAL DIAGNOSIS

Primary adenocarcinoma (Grade II) of transverse colon.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: As Dr. Nathanson has indicated, once having decided that the lesion in the transverse colon was a carcinoma, it is interesting to speculate whether the lesion was a recurrence or a new tumor. The resected specimen of transverse colon, which was 34 cm. long, contained a large annular ulcerated carcinoma 8 cm. in length. The site of the previous well-healed enteroenterostomy was 17 cm. away from the tumor, so that I believe there can be no question that the carcinoma was a new one rather than a recurrence. It was of a moderate degree of malignancy.

Because of the numerous previous abdominal operations, the peritoneal cavity was completely obliterated by adhesions, except for a small area in the right upper quadrant, and the surgeon had a difficult time isolating the proximal transverse colon for resection in order to make sure of the blood supply of the distal portion. Finally, an end-to-side anastomosis between the ascending colon and the sigmoid was performed. No lesion was observed in the descending colon.

The patient left the hospital on the twenty-third postoperative day. Since the regional lymph nodes were not involved, the prognosis should be good.

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MASSACHUSETTS EMIC PROGRAM

WORRY is a dangerous liability to men in combat, and release from the financial exigencies of impending parenthood is one benefit of the Emergency Maternity and Infant Care Program the importance of which cannot be minimized from either the medical or the military viewpoint. More than 1900 Massachusetts physicians have signified their willingness to provide medical care for the 12,184 cases already authorized by the program, which means, as stated elsewhere in this issue of the *Journal*, that more than 10,000 servicemen serving at home and abroad are fighting the war with the assurance of complete, competent medical care

for their wives — not only during pregnancy but also for any acute condition beginning in the first six weeks post partum — and for their infants, including care during sickness and immunization against smallpox, diphtheria and whooping cough. Similarly, the vast majority of Massachusetts hospitals are participating in this wartime service. That all this is greatly appreciated is evidenced by the many letters from servicemen received by the Massachusetts Department of Public Health, which, incidentally, deserves unstinted praise for the way in which the program has been organized and administered in the Commonwealth.

The EMIC program was created to relieve servicemen of the four lowest pay grades of the burden of debt through furnishing this specific type of medical care for their wives and infants, and is not intended to benefit any other group. The rules and regulations were promulgated by the Children's Bureau of the United States Department of Labor, and the states merely act as administrative agencies. The latter are not permitted a great deal of latitude in interpretation except to modify, subject to the approval of the Children's Bureau, regulations that conflict with state laws and practices. All fee schedules used in this program are within the permissive limits set by the Children's Bureau and are subject to the latter's approval.

The original program was planned for the general practitioner, but liberalization of its activities now calls for the services of specialists as qualified consultants. Of course, if a specialist is willing, he may care for a patient as an attending physician.

The EMIC program as a whole and certain of its rules and regulations have been severely criticized and even rejected by several national and state medical societies largely because it is believed that the program is an entering wedge for "state medicine." It should be borne in mind, however, that, in addition to contributing to the morale of the armed forces, the program is an emergency procedure, that, according to the Children's Bureau, it will terminate six months after the war is ended and that, in many sections of the country, it has provided maternal and infant care that would otherwise have been either inadequate or unavailable. The enthusiastic response of the physicians

of Massachusetts attests to their willingness further to assist in the war effort, even though many of them do not approve of certain of the principles involved in this type of medical care. Furthermore, the outcome of the program may provide a means of determining whether this is the type of medical care that the people of the United States want as a steady diet.

"COLD VACCINES"

EACH year as the summer comes to a close and the season for colds begins, persons who regularly suffer from frequent colds and their sequelae seek relief from a recurrence of their difficulties. This is especially true among persons who have had a particularly bad time with colds during the preceding year. Because of the large number of persons afflicted each year, almost every physician is confronted with such cases and has to cope with this problem. Moreover, many physicians are victims of frequent colds, which they are desirous of preventing.

The great majority of physicians frankly admit that they do not know of any method of preventing or reducing the incidence of colds, except perhaps by general hygienic measures, which are thought to "increase resistance" and perhaps also by limiting exposure through contact with persons already manifesting the symptoms of a cold. Neither of these methods can be expected to yield startling beneficial results. Many physicians, on the other hand, state that, although they have no specific means of preventing the colds, the etiologic agent of which is presumably a virus, they are hopeful of preventing the sequelae of colds, which are usually caused by the common bacterial pathogens of the respiratory tract. They therefore resort to vaccines prepared against the more frequent bacteria, namely, pneumococci, streptococci, staphylococci, influenza bacilli and, perhaps, Friedländer bacilli. They hope thus to immunize the sufferers in some specific or perhaps nonspecific way against secondary infections with these organisms.

It is now well known that most of these respiratory pathogens are represented by numerous specific types and that immunity is for the most part type-

specific in character. In other words, it seems futile to attempt immunization against all or even any one group of these organisms. Yet these bacterial vaccines, which are obligingly prepared even by reputable pharmaceutical firms in response to the demand, are regularly given by many physicians in a "shotgun" manner. Carefully controlled clinical experiments on the prevention of colds are difficult to carry out. When they have been done, it is only rarely that any beneficial results from these vaccines have been noted.

In wartime, since colds constitute the major cause of absenteeism from work, their prevention becomes an acute problem. One of the recent attempts to conduct a controlled experiment with commercial cold vaccines has been reported by McGee and his associates* in the Medical Department of the Hercules Powder Company. These industrial physicians used three oral and two parenteral vaccines that are currently offered by commercial laboratories for prophylaxis against the common cold. Their study was carried out in a group of over 1000 industrial and office workers during the October-to-April seasons of 1941 and 1942 and of 1942 and 1943. Placebos were given to some of the subjects, who thus served as controls. Their results are worth quoting:

An examination of the average number of colds suffered per person, the number of days lost per person because of these infections and the number of days lost per infection suggests no outstanding value for any vaccine included in this clinical test. By assigning possible significance to slight differences to the arithmetical averages of the various categories shown in the table, one notes the following: the fewest colds developed in groups receiving either Vacagen, Sharp and Dohme vaccine for parenteral use or a placebo by mouth; groups receiving Oravax, a placebo (orally or hypodermically) or taking no prophylactic medication at all lost fewest days from work because of colds; groups receiving a placebo hypodermically, Oravax or nothing at all have the mildest infections (measured by the length of absence per acute cold reported).

In view of the behavior of the control groups, we find no evidence of clearly effective prophylaxis against either the frequency or the severity (including complications) of the common cold from the use of any of the vaccines studied.

From these studies, McGee and his co-workers conclude, "No clearly evident protection against

*McGee, L. C., Andes, J. E., Plume, C. A., and Hinton, S. H. "Cold vaccines" and incidence of common cold. *J. A. M. A.* 124:555-557, 1944.

the cold and related acute respiratory infections can be demonstrated in the results of this clinical trial at mass immunization." They are therefore led to the further conclusion, "The indiscriminate use of cold vaccines which are now available is not the answer to the problem of industrial absenteeism due to acute respiratory infections." Once again, it has been shown that the administration of "cold vaccines" merely means a waste of the physician's time and of the patient's money.

MASSACHUSETTS MEDICAL SOCIETY COMMITTEE ON PUBLICATIONS

The *Journal* lacks extra copies of the January 13, May 11 and June 1, 1944, issues. Many requests have been made by libraries and other subscribers who wish to bind Volume 230 but who did not receive those particular issues, owing to the difficulties accompanying a change of printers. If any subscribers who do not bind their copies have the January 13, May 11 and June 1 issues on hand, the *Journal* will gladly pay 15 cents for each copy left at or mailed to its office (8 Fenway, Boston 15).

RICHARD M. SMITH, *Chairman*

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

EMERGENCY MATERNITY AND INFANT CARE PROGRAM

More than 10,000 prospective mothers have been accepted for care under the Emergency Maternity and Infant Care Program since it went into effect in Massachusetts last September. The total expenditure for the care of these cases will exceed \$1,500,000, which will be allotted to physicians and hospitals. That this program has proved a boon to the thousands of wives and babies of Massachusetts servicemen in the fourth, fifth, sixth and seventh pay grades is quickly recognized.

Effective August 1, additional physician's services were made available to the wives and infants accepted for care under this program. Each physician will be sent a statement through the mail about the program, and a complete description is available either in the library or in the superintendent's office of each participating hospital. The changes are as follows:

Maternity Care

Medical. The attending physician may receive payment for the treatment of conditions not attributable to pregnancy, both in the home or in the hospital during pregnancy and the post-partum period. Office treatment of intercurrent nonobstetric conditions is included in the overall fee for maternity care.

Surgical. The attending physician may receive payment for surgical conditions not attributable to pregnancy (such

as appendicitis) during the maternity period, which includes a six-week post-partum period, provided that he qualifies as a consultant in a surgical specialty. If the attending physician does not qualify as a consultant in a surgical specialty, he may call a consultant, who will receive payment for any operation he may perform. (There has been no change in the ruling that the attending physician — even though qualified as a consultant — must call another consultant for an obstetric operation if an additional charge for the operation is to be made. No extra fee may be granted to the attending physician for an obstetric operation.)

Continuing care. If a serious acute condition beginning before the end of the six-week post-partum period continues uninterruptedly beyond that period (as in phlebitis), the attending physician may be paid for home or hospital care of this condition continuing beyond the six-week post-partum period. Hospitalization at ward cost, bedside nursing and consultant service may also be paid for under these funds.

Note: All services for which payment is expected must be requested at the beginning of the illness. This request may be made by the physician or hospital by letter or by telephone (CAPitol 4600).

These new services are not retroactive, and payment will not be made for conditions occurring prior to August 1, 1944. Bills for professional services should be sent only after authorization has been received.

Infant Care

Immunizations. Immunizations for smallpox, diphtheria and whooping cough are now included in the program. A maximum payment of \$6.00 for this service will be made to the private physician if no other immunization facilities are locally available. Where immunization facilities are available at local health-department clinics, no payment may be made. If given at pediatric clinics or well-child conferences, the usual clinic fee may be paid, not to exceed the maximum per visit of 50 cents.

Biologicals. Whooping cough, smallpox, diphtheria and combined whooping cough and diphtheria biologicals are furnished free for infants authorized under this program. An addressed postcard requesting biologicals will be attached to the authorization, and this should be mailed directly to the Antitoxin and Vaccine Laboratory by the attending physician.

Crippling conditions. Infants with crippling conditions will be transferred to Services for Crippled Children.

Circumcision. A fee for circumcision is not included under this program.

Consultant Service

Services of a consultant are available provided he meets the standards described in the July 6 issue of the *Journal*, and such services are authorized.

Assistant Service

If no member of the resident hospital staff is available, a private physician may be paid for assisting at a major operation.

BOOK REVIEW

Walter Reed: Doctor in uniform. By L. N. Wood. 8°, cloth, 277 pp., with 18 illustrations. New York: Julian Messner, Incorporated, 1943. \$2.50.

The life of Walter Reed, one of the pioneers in bacteriology in this country, whose fame rests largely on his experiments in Havana, carried out on human beings, which show that the common house mosquito was responsible for the spread of yellow fever, is well known to all members of the medical profession. Mrs. Wood has taken this fascinating story and written it in a simple, straightforward manner, particularly aimed at a popularization of Reed's life for children.

The book is exceptionally well written and should have a wide appeal, for the author is particularly skillful in drawing a picture of an outstanding man in American medicine. The account is accurate, and there is an excellent bibliography, as well as an adequate index. The illustrations are particularly good, and the whole book gives a splendid picture of the man and his accomplishments. It may be highly recommended.

(Notices on page xvii)

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PSYCHIATRIC CASUALTIES OF WAR AND THEIR TREATMENT*

WINFRED OVERHOLSER, M.D.†

WASHINGTON, D. C.

IT IS no exaggeration to say that in the present war the most important medical problem is that of the treatment and prevention of psychiatric casualties. Certainly those who are familiar with the experience of World War I will not be astonished by such a statement. To date the United States Government has spent well over \$1,000,000,000 for the compensation and hospitalization of the nervous and mental casualties of World War I, and even now about 67,000 veterans of that war are receiving compensation for psychiatric disabilities that have been adjudicated as due to service. As a result of the legislative provision that veterans of 1917 and 1918 are eligible for care whether or not their disability is due to service, the psychiatric hospital peak load for World War I has not yet been reached. Whether the rate of incidence of neurologic and psychiatric disorders is greater in this war than it was twenty-five years ago is at the moment uncertain. It may, however, be safely said that on account of the vastly greater size of the armed forces, the number of cases developing must be large. Certain figures published in the January 14, 1944, issue of the *Congressional Record* indicate that out of a total of 3,437,000 registrants rejected from the draft, those rejected for mental disorders constituted 14.5 per cent, those for neurologic disorders 5.4 per cent and those on the ground of mental deficiency 3.3 per cent.

From the experience of World War I it was the hope and expectation that a careful selection of registrants at the induction level would bring about a lowering of the discharge rate for nervous and mental disorder. Unfortunately, that expectation has not been fulfilled. According to the same issue of the *Congressional Record*, the Selective Service System reported that up to January 1, 1944, of the discharges from the Army, 44.6 per cent have been for neurologic and psychiatric conditions. Of these, psychoneurosis led, with 32 per cent of the

discharges. Indeed, the next most frequent cause, schizophrenia — or, as it is sometimes still referred to, dementia praecox — constituted only 4.1 per cent of the total. Epilepsy and neurologic disorders accounted for 2.2 per cent each, and other psychiatric conditions were even less numerous.

The person who leaves civilian life to enter the Army finds himself faced by a number of psychological hazards.¹ One of the greatest of these is the loss of individuality, but there are others. The strict regimentation, the loss of initiative and privacy, the sudden deprivation of dependency on home and family, the sense of loneliness and homesickness, are all factors that are prominent in studies of the psychiatric casualties. The alteration in attitudes toward human life calls for a radical readjustment and reassessment of values. To all these hazards are added, particularly under combat conditions, various physiologic insults caused by mud, vermin, various diseases and loss of sleep and, above all, by sustained fear. Under these added stresses it is perhaps strange that more men do not develop a condition in which their psychological equilibrium can no longer be maintained. On the compensating side it should be pointed out that there are certain constructive phases of military life. The soldier has excitement and change, and he is freed of many of his civilian problems and of the various frustrations of civilian life. If he feels confidence in his leaders and in the cohesiveness of his organization, his own feelings of security and power are increased. It is this mechanism that operates so powerfully under the name of "morale" — perhaps the most important single factor in the rate of incidence of neurosis. There is an identification with the interests of the country in duty and service, and new authority is gained, together with greater maturity. Some neurotic persons, particularly those of an obsessive compulsive type, may fit in particularly well to this picture. Certainly one can say that even though the balance in war is always on the debit side, there are constructive factors, and obviously the majority of men make a

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†Professor of psychiatry, George Washington University School of Medicine, and superintendent, St. Elizabeths Hospital, Washington, D. C.

working adjustment to the stresses that they meet in military life, just as they do to those encountered in civilian life.

Although the psychologic factors involved in the military situation are of a special nature, the reactions to them follow general patterns that are familiar to psychiatrists in civilian practice. Human nature, in short, does not change either in its aims or in its manners of defense. As a general thing it may be said that the psychiatric reactions of war tend to be somewhat more superficial, to run a shorter course and to be more readily amenable to treatment, particularly removal from the specific situation, than is the case with similar types of reaction occurring among civilians.

The psychotic reactions — that is, those reactions that in civilian life would ordinarily call for commitment to a mental hospital — may be dismissed in a comparatively short space. Probably the most frequent psychotic reaction is what is generally diagnosed as acute catatonic excitement or, as Kempf would term it, acute homosexual panic. This condition arises not infrequently in the early days of camp life and is characterized by a sudden onset with marked overactivity, fearfulness, confusion and active auditory hallucinations in which the voices accuse the patient of homosexual practices or inclinations. There may be assaultiveness, and there is frequently refusal of food, which, in connection with the overactivity, may bring about an early dehydration, exhaustion and occasionally even death. It seems likely that many of these reactions are precipitated in latent homosexuals who suddenly find themselves in the midst of large numbers of others of their own sex with little or no privacy. This type of reaction is far from unknown in civilian life, and the recovery rate in state hospitals is not insubstantial. The response to hospital care, particularly with prolonged sedation and interviews with the patient under the influence of Sodium Amytal, is substantially higher and the course, although stormy, is usually brief.² Among the other psychoses are found more rarely depressions, and somewhat more frequently mild manic episodes. These, too, are usually readily responsive to treatment.

Among the psychiatric casualties of war, the psychoses pale into insignificance as compared with the psychoneuroses. In connection with the neuroses an observation may be made about what may be termed "the styles." Just as the *grande hystérie* of Charcot had become practically obsolete by the time of World War I, so it is now found that the trend in the neuroses — at least in the military sphere, and probably in the civilian as well — is away from the conversion hysterias, which were frequent in 1918, in favor of the anxiety states. Anxiety neurosis clearly leads the list among the neuroses. In this condition there is a prevailing mood of worry, with acute attacks of free-floating or un-

fixated anxiety, accompanied by the autonomic symptoms of flushing, sweating, tremors, palpitation and dyspnea, the startle reaction and disturbances of sleep, often accompanied by terrifying dreams. This condition, although not confined to the combat areas, is generally attributed to some catastrophic event, such as an explosion near by, a torpedoing or the death by violence of a comrade. It should always be borne in mind that any person may, if the stress is sufficiently prolonged and sufficiently severe, develop a state of this sort. No one is immune to the neuroses. Often the fundamental conflicts are found not to be the fear of immediate dissolution, but rather to concern domestic situations or other civilian problems, some of which have evidently been in existence for a long period. In general it may be said, just as was found in the follow-up of a group of psychoneurotic patients after World War I, that the more clearly exogenous are the precipitating factors, the better are the prospects. It was found, for example, in 1918 that those victims of neurosis who went back to duty in the largest proportion were those who had been exposed to the concussion of high explosives; their conditions were diagnosed, for example, as concussion syndrome, traumatic syndrome and exhaustion neurosis. A far smaller proportion of those with hysteria were returned to duty than was the case with those with relatively mild and superficial anxiety states that developed following a clear-cut precipitating episode.

Conversion hysteria, which was one of the ordinary conditions in 1917–1918, is relatively less frequent today, although not by any means unknown. A number of conditions, somewhat allied, are grouped under the current heading of "psychosomatic disorders." Effort syndrome, in which one found attacks of dyspnea, sweating, tremulousness and precordial pain, was described by Da Costa soon after the Civil War under the title of "soldier's heart," and was recognized even then as presumably functional in origin. It was frequent in World War I, but is probably somewhat less so in the present conflict. It is generally recognized that a considerable group of gastrointestinal disorders are likewise essentially emotional in origin. This group is not larger entirely on account of the increased diagnostic acumen of the internists, although with the increasing stress now being laid on the importance of psychosomatic medicine this is a factor that cannot be disregarded.

The list of disorders that have been discussed is far from exhaustive, but it represents the principal types of psychiatric casualty likely to be encountered in the military experience. The degree of severity of the symptoms varies, as do some of the specific situations in which certain of the symptoms develop. One thinks, for example, of some of the special problems of aviation medicine, of tank warfare and of fighting in the jungles. The mechanisms, as may

properly be repeated, are fundamentally the same, though the precipitating conditions are different. It is extremely doubtful whether any useful purpose is served by coining new names for these conditions. One hears much nowadays of combat fatigue, fatigue syndrome, flying stress, operational stress and so on, just as one heard of shell shock in World War I.³ These attempts to establish new terminology apparently stem from the idea that there is something inherently disgraceful or improper about the development of a psychoneurosis. If the same amount of energy were put into educating the military and the public concerning the true nature of neurosis as is now devoted to the coining of new names, we should probably be making far more progress!

In a recent issue of a widely read magazine that has never been particularly noted for the accuracy of its medical articles, the readers were informed that there was no curative treatment of psychiatric casualties in World War I, that very few of the men recovered, and that as a result the psychiatric hospitals of the Veterans Administration are now crowded with this "débris of war," whereas a curative treatment has now been developed that is redeeming casualties for combat or useful noncombat duties. The remarks concerning World War I are an interesting example of the manner in which Americans characteristically forget the past. Documentary evidence is readily available that a great deal was done in 1917-1918 in the line of the early treatment of neuroses near the front lines, and it is likewise clear that a very substantial number of men were sent back within ten days or less to front-line duty.⁴ During the Meuse-Argonne drive, for example, 75 per cent of the men treated for war neuroses at the field hospital were returned to duty in an average of four days, and only about 4 per cent of recurrences were found. Rest, occupation and psychotherapy, the very things that are being stressed today, one finds emphasized then. This is not to say, however, that no progress has been made in the line of therapy. Much, indeed, of a constructive nature has taken place.

Much has been learned since World War I of the psychologic mechanisms of these casualties, and there have been learned, too, several new approaches to the patient that enable psychotherapy to be more effective. Among the newer methods perhaps the most significant is what has been variously termed "narcoanalysis" and "narcosynthesis" or "Amytal interviews." The first term was invented by Horsley⁵ in 1936, and the second has been utilized more recently by Grinker⁷ in describing his significant work in the North African campaign. The treatment consists in the intravenous administration of Sodium Amytal or Pentothal Sodium in a dose sufficient to bring about a moderate degree of narcosis (5 to 7½ gr.). This treatment is a valuable aid in releasing inhibitions, overcoming the

resistance of the patient and enhancing his suggestibility. It may be utilized in the treatment of the neuroses and even of the psychoses, particularly when the patient is inaccessible. It provides an access to the deeper layers of consciousness, and not infrequently a patient talks freely who without the drug would be completely mute. In the stage of suggestibility brought about immediately after the administration of the drug, hysterical symptoms may be caused to disappear, and it can then be demonstrated to the patient that his disability is not a permanent one. Narcoanalysis is a valuable procedure that is being widely used with great success. It requires no apparatus except the hypodermic syringe, can be utilized at points near the front lines and has been used in a large number of cases in restoring soldiers to active duty. It should always be remembered, however, that the drug constitutes merely a useful adjuvant to psychotherapy. The important feature of this method of treatment is the increased accessibility of the patient to the ministrations of the therapist; to this extent, it really should hardly be classified among the drug therapies.

Continuous narcosis treatment calls for hospital facilities and a good deal of nursing attention. It has not been so promising as was hoped when it was first introduced, and it is likely that the simpler method of narcoanalysis provided all the benefits, except that in cases of profound exhaustion the continued narcosis provides a long period of much needed rest.

A few words should be said about the various types of what Strecker⁸ has aptly termed "the drastic therapies." Insulin-shock therapy is not especially applicable in these cases, although Sargant⁹ has used what he terms "sub-shock insulin therapy" and has found it useful as a general tonic in cases of war neuroses, and also as a sedative therapy in excited states. The Metrazol treatment of Meduna has been found to have certain disadvantages and has been almost entirely replaced by the electric-shock treatment of Cerletti. The latter has been particularly useful in the treatment of the depressions, and is therefore applicable largely in general or station hospitals rather than nearer the front lines. In the depressions there is always danger of suicide, hence any treatment that shortens the course of the disorder not only benefits the patient but results in a saving of available man power among the hospital personnel. The electric-shock method is not without risk, however, and should not be employed without the precaution of a thorough physical examination, in addition to x-ray examination of the chest and spine, and preferably (at least in patients past thirty) an electrocardiogram. Obviously physiologic changes take place when the electric current is passed through the brain of the subject. I find it hard, however, to agree with Myerson¹⁰ who has stated

categorically that the value of shock treatment does not appear to have a psychologic foundation. He proceeds to say, rather, "Physiologic alterations of an unknown type take place and this is the basis of the recovery." To many of us one of the values of the shock treatments in general and of electric-shock in particular has seemed to be that it placed the patient in an especially dependent situation with relation to the physician, and that in turn it directed the physician's attention to the needs of the patient, thus bringing about a closer rapport. Indeed, electric-shock or other shock therapy, without psychotherapy, — that is, the impact of the personality of the physician on the patient, — is likely to fail of its full effect. There is no royal road, even an electrical one, to the cure of mental disorders, but there is no doubt that electric-shock therapy has been of great value, particularly in the treatment of the depressions. It has likewise been found useful in acute maniacal conditions.

Years ago Pratt¹¹ demonstrated effectively what could be done in the line of group therapy. The work that he started is being confirmed and developed in many different ways today. Psychotherapy is a time-consuming process. The number of persons who need it is large, and the floating supply of psychiatrists is small. Two things must be done if adequate treatment is to be given to the patients being considered. One is to develop in nonpsychiatrists an appreciation of the importance of emotional conflict and the need and the value of psychotherapy. The other is to arrange for the treatment of groups of patients, thus multiplying for practical purposes the amount of time that the therapist may employ per patient. Group discussions are being used at various centers with substantial success, and at a few points a specialized form, the psychodrama, has proved successful.

Among other forms of therapy one certainly must not fail to mention occupational therapy, a form that was utilized overseas during World War I, and which is again being developed by the Army. It seems probable that its value will eventually be fully recognized again, as it was in 1918. Various physiotherapeutic approaches, some of which have already been mentioned, are of value, partly on account of the physiologic changes brought about by them, and partly on account of the psychologic factors involved.

Time does not permit a more detailed consideration of a long and complicated subject. Enough has been said, however, to indicate that although the incidence of psychiatric casualties is substantial,

the prognosis, both for the psychoses and for the neurotic manifestations, is better than one would expect to find with similar symptoms in civilian life.

What of the future? One of the greatest defects of public education at the moment is shown in the lack of the proper attitude toward the psychiatric dischargee and rejectee. The attitude of the family, the attitude of the employer and the attitude of society as a whole leave much to be desired. Too many persons fear the man who is known to have suffered a psychiatric disability in service. They fear that he is a "raving maniac," that he is unsafe to have about, that he is so changed a person that he should be looked on as a pariah. There are employers who refuse to re-employ a man known to have been discharged for a psychiatric cause. Such a situation is tragic and must be rectified if the improvement of these men is to be maintained. If the dischargee comes home to find himself rejected, he loses confidence and may readily suffer a relapse. One may question also what the effect of the generous compensation laws enacted by Congress is to be. It may well be that cases will be kept active because recovery is to be penalized by loss of a fixed income. In this regard war casualties of a psychiatric nature are likely to be similar to unsettled industrial-compensation cases. If lump-sum settlements could be arranged, it is likely that greater inducement would result for the recovery of the patient. Finally and most important, if these men on returning can be made to feel that they are respected, that they are wanted, that their place in the community is secure and that work is available for them, we may safely dismiss any fears that we are to be overwhelmed by a flood of permanent psychiatric casualties of war.

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POTASSIUM BICARBONATE: AN ADJUNCT TO CHEMOTHERAPY IN PNEUMONIA COMPLICATING CARDIAC DECOMPENSATION*

A Preliminary Report

JOHN OHNSTY, M.D.,† AND WILLIAM QUITMAN WOLFSON, M.D.‡

BROOKLYN, NEW YORK

A COMPLICATION frequently encountered in the administration of sulfonamides is kidney damage. If adequate urinary output is maintained and the urine is kept alkaline, the incidence of crystalluria, hematuria and frank renal damage is decreased.^{1,2} These measures are particularly important in patients with marked cardiac insufficiency, who tend to retain ingested water and to excrete small amounts of urine.

Sodium bicarbonate is most frequently used for alkalization. Modern therapeutics, however, stresses the primary significance of sodium retention in the development of cardiac edema and congestive heart failure.³⁻⁷ In cardiac decompensation, a regime promoting a negative sodium balance is considered advisable; it is not aided by the administration of sodium bicarbonate.

In the medical wards of this hospital are many patients in whom pneumonia accompanies and often precipitates cardiac decompensation. Rational therapy requires that both be treated simultaneously. This involves the administration of sulfonamides, the maintenance of adequate urinary output, urinary alkalization, restriction of sodium intake and promotion of diuresis, as well as the employment of other recognized measures.

Because the administration of sodium bicarbonate was considered to be incompatible with these objectives, other alkalizing agents were investigated. Many were tried and found to be unsatisfactory because of their tendency to cause gastrointestinal upsets when used in sufficiently large amounts. Potassium bicarbonate was finally chosen for clinical trial, since it was well tolerated in required doses.

METHOD OF STUDY

A group of patients with severe cardiac impairment and pneumonia treated with sulfadiazine and potassium bicarbonate were compared with a similar group treated with sulfadiazine and sodium bicarbonate. All the cases studied were admitted to the medical wards of the Greenpoint Hospital between December 1, 1943, and March 1, 1944. The criteria for inclusion in the study were survival for at least seventy-two hours after admission, cardiac decompensation of sufficient severity to be classified Grade III or IV according to the

specifications of the American Heart Association,⁸ demonstration of a lobar or bronchopneumonic process by clinical and radiologic findings and the absence of findings suggesting severe renal impairment or adrenal insufficiency. The last criterion was adopted as a precaution against potassium toxicity. Patients treated by us were given potassium bicarbonate; those treated by the other members of the house staff were given sodium bicarbonate.

All patients were given an initial dose of 4 gm. of sulfadiazine, followed by 1 gm. every four hours. In addition, they received an initial dose of 8 gm. of sodium or potassium bicarbonate, followed by 2 gm. of the chosen agent every four hours. To both groups fluids were given freely, and the patients were encouraged to drink at least 2500 cc. per day. Daily fluid intakes and outputs were measured, and the urinary pH was determined daily from a 6 a.m. specimen by the nitrazine method. Because of the difficulty of obtaining serum potassium levels, these could not be studied. In addition, many patients were critically ill and weight variations were unobtainable. Further routine orders included complete bed rest, a soft, low-salt, 1200-calorie diet, digitalization and other symptomatic measures as indicated, except diuretics.

RESULTS

Sixteen patients were studied over a total of sixty-five hospital days. Nine patients were treated with potassium bicarbonate (Table 1) and 7 with

TABLE 1. *Average Daily Fluid Intakes, Outputs and Intake-Output Differences for Patients Treated with Sulfadiazine and Potassium Bicarbonate.*

CASE No.	SEX	AGE	PERIOD TREATED	FLUID INTAKE	FLUID OUTPUT	INTAKE-OUTPUT DIFFERENCE
		yr.	days	cc.	cc.	cc.
1	M	66	9	1390	1010	380
2	M	22	3	1620	1010	610
3*	M	69	4	1310	1100	210
4	F	82	5	2090	990	1100
5	F	49	3	3400	1340	2060
6	F	54	7	2970	2820	150
7	F	62	5	2520	910	1610
8	F	46	4	2460	1430	1230
9	F	56	3	1610	1380	230
Averages		56.2	4.2	2152	1332	820

*Patient died.

*From the Department of Internal Medicine, Greenpoint Hospital, Brooklyn, New York.

†Formerly, assistant resident physician, Department of Internal Medicine and Department of Pediatrics, Greenpoint Hospital.

‡Formerly, intern, Greenpoint Hospital.

sodium bicarbonate (Table 2). The intakes, outputs and differences between the two for the two groups are compared in Table 3.

Maintenance of alkalinity. The 6-a.m. urine was chosen as the likeliest to be acid, and was taken immediately after awakening, thus avoiding the so-called "morning alkaline tide" of the urine, which

TABLE 2. *Average Daily Fluid Intakes, Outputs and Intake-Output Differences for Patients Treated with Sulfadiazine and Sodium Bicarbonate.*

CASE No.	SEX	AGE	PERIOD TREATED	FLUID INTAKE	FLUID OUTPUT	INTAKE-OUTPUT DIFFERENCE
		yr.	days	cc.	cc.	cc.
10	M	31	5	1150	720	430
11	M	48	3	2680	1000	1680
12	M	38	3	2030	940	1090
13	M	70	3	1430	260	1170
14	M	76	7	1560	980	580
15*	M	61	2	2430	620	1860
16*	M	81	4	1700	830	870
Averages		60.7	3.9	1861	764	1097

*Patient died.

is induced by the respiratory readjustments consequent on awakening. In only two of sixty-five samples studied was an acid urine found, and in a great majority a reaction of pH 7.4 or higher was

TABLE 3. *Comparison of Intakes, Outputs and Intake-Output Differences of Patients Treated with Sulfadiazine and Sodium or Potassium Bicarbonate.*

TYPE OF PATIENT	FLUID INTAKE	FLUID OUTPUT	INTAKE-OUTPUT DIFFERENCE
	cc.	cc.	cc.
Potassium-treated patients	2152	1332	820
Sodium-treated patients	1861	764	1097
Differences	291	568	-277
Percentages (K:Na)	116	174	75

maintained. The dosage of bicarbonate was not increased for patients not showing a urine of pH 7.4, but in further studies it is intended routinely to increase the dosage by 25 per cent to ensure alkalization.

Fluid intake. In most cases, it was not possible to achieve the desired daily intake of 2500 cc. The average fluid intake of patients treated with potassium bicarbonate was 2152 cc., and that of those treated with sodium bicarbonate was 1861 cc. The potassium-treated patients thus ingested an average of 291 cc. more than those in the control group.

Fluid output. No patient treated with sodium had an average daily output of over 1000 cc., whereas 7 of the 9 potassium-treated patients exceeded this figure. The average daily output was 1332 cc. in the potassium-treated group, but only 764 cc. in the sodium-treated group. Although, on the average, the former patients consumed 291 cc. more liquid than did the latter, they excreted 568 cc. more daily.

Intake-output differences. Since both groups of patients were maintained under identical conditions of diet, bed rest and environmental temperature,

any differences due to amounts of metabolic fluid derived from food and to quantities lost during respiration, from the skin and in the feces were not important and tended to offset each other.⁹ Under these conditions the patients showing a marked difference between intake and output were either retaining fluid in the body or excreting body fluid less rapidly than the others. If the body weights of both groups were gradually decreasing, it could be assumed that the observed intake-output difference was due to greater diuresis in one group than in the other.

Since most of the patients recovered from their congestive failure, it seems probable that the observed intake-output difference between the sodium-treated and potassium-treated groups depended on more rapid elimination of retained water by the latter. Unfortunately, daily weight determinations were impractical.

In this series the average difference between intake and output was 820 cc. a day for the potassium-treated patients and 1097 cc. for those treated with sodium. If the difference of 277 cc. a day between the two groups is interpreted as indicating more rapid excretion of excess water by the potassium-treated patients, this means that over the average period of treatment these patients excreted an average of 1250 cc. more retained fluid than did the sodium-treated patients. Only once in the sodium-treated group was the daily urinary output greater than the fluid intake, but outputs greater than intake were observed in one fifth of daily observations in the potassium-treated group.

DISCUSSION

There has been increasing realization that alkalization of the urine and maintenance of a satisfactory fluid output are essential during the administration of sulfonamides.^{1, 2} Approximately 1 per cent of patients receiving sulfadiazine show a significant increase in nonprotein nitrogen blood levels¹⁰; hematuria and crystalluria are frequent. Sodium bicarbonate given in doses equal to those of sulfadiazine and sulfathiazole reduces the incidence of crystalluria by 60 per cent. The amounts of sulfadiazine and of acetylsulfadiazine dissolved in normal urine at pH 7.5 are twenty times greater than those dissolved at pH 5.0.² Despite its theoretical advantage, sulfamerazine is not appreciably less nephrotoxic than sulfadiazine.¹¹ Alkalization is usually accomplished by giving 12 to 18 gm. of sodium bicarbonate a day. In most normal subjects the fluid output can be satisfactorily established at over 1000 cc. by an intake of 2500 to 3500 cc. a day.

The low-salt diet given these patients contains about 1.5 gm. of sodium a day. When 12 to 18 gm. of sodium bicarbonate are given daily, another 3.5 to 6.0 gm. of sodium is added. A patient with severe cardiac disease kept on a low-salt diet but

given sulfonamide and sodium bicarbonate receives from 5.0 to 6.5 gm. of sodium each day. This is appreciably larger than the 2-gm. to 4-gm. sodium content of the average American daily diet. Despite general recognition of the importance of sodium restriction in preventing and treating cardiac decompensation, the danger of administering such large doses of sodium bicarbonate to patients with severe heart disease has not been completely discussed by the advocates of alkali therapy.

The physician attempting simultaneous treatment of severe cardiac lesions and pneumonia has had to choose from several difficult alternatives. Sulfadiazine and sodium bicarbonate have been given, achieving alkalinization but risking the impeding of treatment directed toward improving the cardiac status and seriously decreasing the urinary output. Prescription of sulfadiazine without sodium bicarbonate is more considerate of the failing heart, but urinary acidity increases the threat of renal damage. If the fluid intake is limited to the amount required to overcome water retention induced by administered sodium, dangerous minimal fluid outputs result. Under satisfactory conditions patients with severe heart damage tend to have a small urinary output; under stress of infection the output may decline appreciably. This makes alkalinization indispensable when chemotherapy is given to such patients.

The efficacy of potassium bicarbonate in promoting adequate urinary output and rapid elimination of retained water depends on the special differential metabolism of sodium and potassium in cardiac decompensation. The primary factor involved is apparently the tendency of patients with chronic congestive failure to retain sodium.⁴ The cause is either endocrine or, more probably, renal; the exact mechanism is not understood, but essentially in all patients there is inability of a functionally damaged heart to meet the metabolic demands of an active person. With retention of sodium, water is held to maintain the constancy of the body's electrolyte pattern and, more importantly, the pattern of the extracellular fluid. Both the plasma volume and the volume of the extracellular, extravascular compartment are increased. Dilution of plasma proteins leads to increased production, with maintenance of normal oncotic pressure. Eventually, a continual increase in plasma volume leads to engorgement of the entire vascular bed, producing increased venous pressure, edema and clinical congestive phenomena. In acute cardiac decompensation other factors lead to increased venous pressure.³⁻⁵ In these patients, both acute and chronic factors were usually clearly implicated.

Pulmonary engorgement, deficient nutrition and the poor resistance of waterlogged, improperly oxygenated tissue lead to increased susceptibility to pneumonic processes. These infections induce secondary factors that further decrease cardiac

efficiency. Toxic myocarditis may reduce the already minimal cardiac reserve, and increased respiratory effort and accelerated metabolism of fever increase the load that must be borne. Lung involvement may lead to poor blood oxygenation, with resulting impairment of all oxidative processes, including those of the heart.

During pneumonia there is a decreased chloride output,^{12,13} and with this retention of fixed acid there is a concomitant tendency to retain fixed base. Since sodium is the most important mobile fixed base,¹⁴ this further accentuates the tendency to its retention, and decreases in sodium output result. Moreover, electrolyte concentrations of the extracellular fluid, particularly in lobar pneumonia, are temporarily stabilized at lower values.¹⁵⁻¹⁷ Even if no additional sodium were added to the body stores, additional water could be retained because of decreased sodium concentration per unit volume. It is not surprising that pneumonia so frequently causes striking impairment of the status of patients with injury to the heart.

Unlike sodium salts, which favor water retention, the salts of potassium have a definite diuretic action.^{7,18-20} Both in the normal state and in decompensation, ingested potassium is rapidly and quantitatively excreted, carrying water with it. The excretion of sodium is also somewhat accelerated because the sodium-conserving ability of the kidney is not absolute and because, with elimination of water, a certain amount of sodium must be excreted to defend the electrolyte pattern of the extracellular fluid.¹⁴

Reports of toxic effects attributable to therapeutic doses of potassium are infrequent, and no signs of intolerance were noted in this series. The oral administration of 40 gm. per day to patients with myasthenia gravis has produced no untoward effect.²⁰

The normal serum potassium level is from 3.4 to 4.8 milliequiv. per liter²⁰; elevated levels have been reported in shock, asphyxia, hemorrhage, intestinal obstruction and fistula, crush syndrome, pemphigus, severe adrenal insufficiency and uremia.²⁰⁻²² Only the latter two had to be considered in this study, and patients in whom either was suspected were excluded. In addition, electrocardiograms were studied, urinary outputs were carefully watched and pulse rates were frequently charted. The patients were observed and questioned about attacks of weakness and gastrointestinal disturbances. Potassium was to be discontinued if electrocardiographic changes, a pulse rate below 70, a urinary output below 600 cc. or an attack of weakness or gastrointestinal intolerance occurred; fortunately, it was never necessary to apply this rule.

In Addison's disease, there is a tendency to lose sodium and to retain potassium²³; if the salt intake is restricted and potassium is given, an acute exacerbation results.²⁴ Although patients were excluded

in whom adrenocortical insufficiency was suspected, it is unlikely that our regime could have induced acute adrenal crisis in the decompensated cardiac patients. Such persons to some extent have an electrolyte metabolism opposite to that of the Addisonian; they have ample sodium reserves, their adrenal glands are not impaired, and they tend to sodium retention rather than to sodium depletion.

Toxic effects have been reported in severe renal insufficiency when potassium was given; these consisted of intermittent bradycardia, attacks of weakness and electrocardiographic findings of partial heart block with T-wave inversions.²⁵ Retention of potassium in uremia is not due merely to the extreme renal damage, for a case has been reported in which uremia was accompanied by potassium depletion.²⁶ The situation is somewhat analogous to that of renal rickets; in the usual form, there is hyperphosphatemia and hypocalcemia, but rarely hypercalcemic renal rickets is seen.²⁷ A complex metabolic disturbance occurs in renal insufficiency, but for our purposes it was felt safest to exclude these cases.

If subsequent employment of mercurial diuretics is contemplated, alkalization is terminated as soon as possible in order not to decrease their efficiency.^{28, 29}

Actually, the 12 gm. of potassium bicarbonate given each day represents less potassium than the 10 gm. of potassium chloride frequently used as a daily diuretic dose. Together with the low reported toxicity, adverse effects seem unlikely even without the precautions adopted in this study.

SUMMARY

Potassium salts have long been used as diuretics. Employing conventional dosage, we have attempted to utilize the diuretic effect of potassium and the alkalizing effect of its bicarbonate to facilitate treatment of patients with severe heart damage who were receiving sulfadiazine for pneumonia. Patients so treated drink somewhat more liquid than do those given sodium bicarbonate, but they excrete almost twice as much urine and eliminate over 250 cc. more of retained fluid each day. By promoting excretion of retained water and sodium, potassium facilitates the re-establishment of cardiac compensation.

At present, we give potassium bicarbonate to all patients whose cardiovascular status is classified as Grade III or IV whenever they receive sulfonamides. Its use is being extended to milder cases as pro-

phylaxis against decompensation. Ten grams given with the initial dose of sulfonamide and gm. every four hours thereafter until twenty-four hours after discontinuance of chemotherapy.

Although apparently of low toxicity, potassium bicarbonate is not used when severe renal impairment or adrenocortical insufficiency is suspected.

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FULMINATING MENINGOCOCCEMIA

Demonstration of Intracellular and Extracellular Meningococci in Direct Smears of the Blood

WILLIAM P. BOGER, M.D.*

BLUEFIELD, WEST VIRGINIA

IT IS the purpose of this paper to call attention to the unusual finding of meningococci by direct examination of the peripheral blood smear, in a case of fulminating meningococcemia that may also have been a case of the Waterhouse-Friderichsen syndrome.

CASE REPORT

A 27-year-old woman (M. C. V. A-18280) was admitted to the hospital on January 29, 1943. She stated that she was traveling by bus from Atlanta, Georgia, to Elmira, New York, when she began to feel "sore all over," apparently from sleeping in a cramped position. In the course of a few hours there developed a dull headache, stiffness of the neck, slight nausea and finally persistent vomiting. Because of the vomiting the patient left the bus and presented herself at the Emergency Ward of the hospital.

The patient was able to give a clear account of herself, and stated that prior to 8 hours before admission she had been perfectly well. The only significant point in the recent history was the ingestion of ground meat 2 days previously.

Examination showed a well-developed and well-nourished woman lying comfortably in bed. The temperature was 102° F., the pulse 90, the respirations 20, and the blood pressure 100/60. The pupils were equal and reacted to light and accommodation. The ocular fundi showed no papilledema. The pharynx was slightly injected and the patient mentioned a slight feeling of scratchiness. The chest was clear. The heart was normal in size, rate, rhythm and sounds. The neck was supple and no stiffness was noted. The reflexes were equal and active, the Kernig and Brudzinski signs were absent, and the Babinski responses were plantar. The muscles of the entire body were tender on palpation, especially in both lower legs. There was no edema.

The patient appeared to be suffering from influenza, but the diagnoses of trichinosis and meningococcal meningitis were also entertained. Trichinosis was considered because of the ingestion of ground meat of questionable origin, and meningitis because of the prevalence of meningococcal infections.

Examination of the blood revealed a hemoglobin of 76 per cent (Sahli). The white-cell count was 11,900, with 99 per cent neutrophils, most of which showed marked toxic granulation. A lumbar puncture was done in the 4th lumbar interspace and clear fluid under 100 mm. of water pressure was obtained. The cell count was 7 lymphocytes per cubic millimeter. No organisms were seen on microscopic examination of the fluid.

Four hours later a venipuncture was done to obtain a specimen for routine chemical study, and during this procedure several petechiae were noticed on the forearm. No other petechiae were observed, and in view of the normal spinal-fluid findings no significance was attached to this observation.

The following morning the patient was obviously more ill, complaining of severe pains in the muscles and joints and presenting a generalized purpuric rash, with lesions varying in diameter from 0.5 mm. to 2 or 3 cm. These lesions were not raised above the surface of the skin, were nontender and did not fade on pressure. The larger lesions were deep purple, and several lesions of this type were located at the fingertips, simulating closely the appearance of gangrene. Purpuric spots were present over the face, the extremities, the body, the conjunctivas and the oral mucous membrane. A diagnosis of fulminating meningococcemia was at once made. The patient was still mentally alert but was

frankly apprehensive, whereas the night before she had regarded herself as only mildly ill.

A blood specimen was taken for culture and examination and at the same time 10 gm. of sodium sulfadiazine was given intravenously. The temperature was 103° F., the pulse 110, and the respirations 24. The white-cell count again revealed 99 per cent neutrophils. There were few adult neutrophils as compared with the number of premature forms, and on stained smears, 7 per cent of the polymorphonu-



FIGURE 1. Photomicrograph of a Polymorphonuclear Leukocyte Containing Phagocytized Meningococci (x900).

clear cells were found to contain phagocytized gram-negative diplococci (Fig. 1). Extracellular organisms were also observed.

At noon the patient was given a 500-cc. transfusion. Antimeningococcus serum was not available. An infusion of 1500 cc. of 5 per cent glucose in physiologic saline solution was given, but the patient became steadily worse. The temperature declined, the pulse rate rose, and the blood pressure fell to 60/40. Four cubic centimeters of cortical extract was given intramuscularly. The purpuric spots previously noted were seen to enlarge and new petechiae appeared.

That evening the patient presented a startling appearance. Intracutaneous extravasations too large to be covered by the outspread hand were present over the thorax and extremities, and extravasations of smaller size were present on the face. The patient could not be roused. The temperature was 99° F., the pulse 140, and the respirations 30. It was believed that the patient presented the classic clinical picture of the Waterhouse-Friderichsen syndrome.

During the night she gradually went into a state of vasomotor collapse, and in spite of further infusions of 5 per cent glucose in physiologic saline solution and 2 cc. of cortical extract, she died at 6.25 a.m. on the following day.

Permission for autopsy was not granted, so that doubt remains whether there were adrenal hemorrhages, as required to fulfill the criteria of the Waterhouse-Friderichsen syndrome. The duration of the illness was approximately 47 hours.

The diplococci seen in the blood smears were cultured from the blood stream and found to be meningococci.

DISCUSSION

Fulminating meningococcemia runs its course in a matter of hours, usually less than forty-eight. Of this form of meningococcal infection, Herrick¹ has

*Director, Medical Department, St. Luke's Hospital, Bluefield, West Virginia; formerly, medical resident, Medical College of Virginia, Hospital Division, and instructor in medicine, Medical College of Virginia, Richmond.

said, "No other infection so quickly slays." In this disease the diagnosis must be made as promptly as possible and treatment instituted at once, for if the development of the clinical picture is awaited, the hope of survival is negligible. The length of time required for blood cultures reduces their value as a clinical aid²; as in this case, they are frequently of only academic and post-mortem interest.

McLean and Caffey³ found meningococci in smears taken from the petechiae and purpuric extravasations seen in many cases of meningococcal infection. This procedure is simple and should be oftener resorted to. Unfortunately, many cases of meningococcal meningitis fail to develop a rash, and in fulminating meningococcemia the type of purpura is in itself almost diagnostic.

Herrick⁴ and Adams² cursorily mention the finding of meningococci in the peripheral blood. Boone and Hall,⁵ Marangoni and D'Agati,⁶ and Kwedar⁷ have encountered cases and presented photographs of meningococci in the peripheral blood. Thomas⁸ mentions that in 6 of 12 fatal cases of fulminating meningococcemia organisms were seen in the peripheral blood. It is thus seen that a diagnosis from the blood smear is possible.

It is not suggested that every blood smear made in an acutely ill case should be scrutinized for phagocytized gram-negative organisms, but such examination is worth consideration when there is meningitis in the community, when there is objective muscle tenderness, and when a gripe-like or influenza-like syndrome is presented in combination with a leukocyte count that is predominantly polymorphonuclear. With reference to these points, it is impossible to be too alert in suspecting meningococcal infections when the disease is established in a community. The muscle tenderness that was present in this case was not sufficiently appreciated, but from observation of other cases of meningococcal septicemia it is apparent that Dickson et al.⁹ are correct in their statement that this is a symptom that differentiates meningococcal septicemia from other forms of acute infection. The type of the tenderness is clearly different from the myalgia complained of in the usual case of acute febrile illness. The leukocytic response is likewise instructive, and Herrick⁴ says, "Excepting lobar pneumonia no other acute infection is accompanied by such early and profound leukocytic reaction, 50,000 to 60,000 with an average of 90 per cent polymorphonuclears."

Its use as a bacteremia so overwhelming as to present free in the blood stream in such numbers can be found on a direct blood smear hope of recovery. The finding has been only in fatal cases.⁵⁻⁸ As has been pointed out, if routine examination of the blood could establish the diagnosis, valuable time and therapy instituted in time to save the patient.^{5, 6}

The suggestion that the examination of the direct blood smear in the occasional case may be worthwhile has added weight inasmuch as, according to Thomas,⁸ "It seems fairly certain now that every clinical meningococcal infection with the possible exception of a variety of infection of the upper respiratory tract consists at some stage of an invasion of the blood stream by the causative organism." This concept is only now being generally accepted, but Herrick⁴ clearly stated it in 1915. Indeed, the blood stream may be the only site of the infection. "Three patients," he states, "each having a blood culture positive for meningococci of Group I, recovered spontaneously without drug or serum therapy before the culture was known to be positive."

In speaking of fulminating meningococcemia, the subject of the Waterhouse-Friderichsen syndrome is called to mind. The terms are not synonymous. The Waterhouse-Friderichsen syndrome is an overwhelming septicemia that produces purpuric subcutaneous extravasations and bilateral adrenal hemorrhages. Although it is true that meningococcal infections usually produce this syndrome, overwhelming sepsis due to other organisms occasionally gives rise to similar adrenal hemorrhages. Furthermore, not all patients who die with the clinical picture of the Waterhouse-Friderichsen syndrome present adrenal hemorrhages. Thomas⁸ remarks their absence in 6 of 23 autopsied cases. Hence it seems ambiguous to use the term "recovery" in speaking of the Waterhouse-Friderichsen syndrome since the adrenal hemorrhages can only be inferred if the patient recovers. Clinically the term "fulminating meningococcemia" seems preferable to "Waterhouse-Friderichsen syndrome," and if the latter has any usefulness it should be restricted to pathological discussions.

The bilateral adrenal hemorrhages seen in these fulminating septicemias have suggested that the mechanism of death is that of acute adrenal failure. The hypotension, hypothermia or hyperthermia, vascular collapse, abdominal pain, vomiting and cadaveric cyanosis — incident to the intracutaneous extravasations — are indeed similar to the findings in the crisis of Addison's disease. There are, however, in the literature no significant data concerning electrolytes, blood sugar, nonprotein nitrogen and hematocrit readings in cases of fulminating septicemia. Aegerter¹⁰ in reviewing the subject of the Waterhouse-Friderichsen syndrome calls attention to the paucity of such data. This is not to be wondered at, since the short course of the disease, the uncommonness of the cases in adults and the imperativeness of treatment leave little time for investigation. In the case reported herein the blood sugar was 89 mg. per 100 cc., and the nonprotein nitrogen 44 mg., the latter figure being somewhat elevated. It seems doubtful that changes in electrolyte or carbohydrate metabolism drastic

organisms that they offer little reported on however can be

enough to produce death would occur in a matter of an hour or two. Especially doubtful does this explanation of death become when one considers that the experimental animal withstands complete surgical ablation of the adrenal glands for a much longer period than the forty-eight hours that is usually set as the upper limit of survival in fulminating meningococcemia.

On the other hand, the suggested treatment of these cases with massive doses of cortical extract, adrenalin, intravenous glucose and saline solutions and blood transfusions¹⁰ seems worthy of trial. This type of therapy was used in the present case, but the amount of cortical extract was insignificant and the amounts of intravenous fluids were small. Loeb¹¹ states that 50 to 75 cc. of commercial cortical extract must be used every twenty-four hours in the treatment of crisis in Addison's disease, and a comparable dosage seems to be indicated in treating fulminating meningococcemia.

The hypothesis that death is due to acute adrenal failure is attractive but not proved. The additional fact that some patients die of fulminating meningococcemia without showing adrenal hemorrhages indicates that however undesirable the term "toxemia" is, there is still a place for this concept. In a bacteremia with organisms free in the blood stream in enormous numbers the products of their metabolism in terms of toxins are certainly appreciable, which suggests that antibacterial and antitoxic serums should be used in these cases. Thomas,⁸ although admitting that the subject is controversial and that the majority opinion is indifferent to the use of antiserum, states, "There is one group of patients who seem to have been benefited by meningococcus antitoxin, namely, . . . [those with] septicemia."

It may yet be established that the subcutaneous extravasations seen in cases of fulminating meningococcemia are due to a vascular toxin. Thrombosis of small vessels in the adrenal glands by clumps

of meningococci has been demonstrated, but proof that the skin lesions are due to a similar mechanism has not been forthcoming.

SUMMARY AND CONCLUSIONS

A case of fulminating meningococcemia has been presented.

The term "Waterhouse-Friderichsen syndrome" appears to be ambiguous when applied to the living patient.

The concept of acute adrenal failure as the mechanism producing death is attractive, although not proved, but certain measures of therapy useful in combating the crisis of Addison's disease may, nevertheless, be applicable in fulminating meningococcemia.

In this type of meningococcal infection antiserum should probably be used.

In certain cases the examination of the blood smear may establish the diagnosis more promptly than is possible by any other means.

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MEDICAL PROGRESS

THORACIC SURGERY (Concluded)

JOHN W. STRIEDER, M.D.*

THE ESOPHAGUS

ALTHOUGH the esophagus has been called "the last frontier of surgery," notable advances have been made in the surgical treatment of various lesions of this organ since the publication of the excellent and exhaustive review of the subject by Bird⁴⁸ that appeared in 1939. The achievements in congenital atresia and carcinoma have been outstanding.

Congenital Atresia

Vogt⁴⁹ classifies the anomaly of congenital atresia as follows: complete absence; atresia without tracheal fistulas; atresia with fistulas between the trachea and the esophagus, situated between the upper segment and the trachea, between the lower segment and the trachea or between both segments and the trachea. In this classification the second and particularly the third type constitute the great majority of reported cases that are being treated surgically with increasingly encouraging results.

The constant symptoms, consisting of regurgitation of milk and mucus with attacks of choking, cyanosis and coughing, occur when the infant is first fed. A plain roentgenogram of the abdomen shows the stomach filled with air, thus proving the presence of tracheoesophageal fistula, which occurs in about 75 per cent of the cases of atresia, as distinguished from the far less frequent complete or incomplete atresia of the esophagus without a fistula which occurs in 25 per cent.⁴⁸ As suggested by various authors,^{50,51} diagnosis can be verified simply and safely by passing a small catheter into the esophagus. This proceeds readily into the stomach in any normal infant. If it meets obstruction at the level of the thoracic inlet, — this may be verified by fluoroscopy, — the diagnosis can be definitely made. With diagnosis thus established, attempts to visualize the blind pouch by injecting barium or iodized oil should not be made, since they almost always result in the introduction of opaque material into the lungs, with resultant pulmonary complications. Once the diagnosis is made, unless there are other anomalies that contraindicate operation, this should be proceeded with at the earliest feasible moment to prevent the frequent complication of aspiration pneumonia.

Although the ideal treatment is the ligation and division of the fistula with re-establishment of

esophageal continuity, this cannot always be achieved, and other and indirect measures have been devised and successfully carried out to meet such situations. To Leven⁵² must go the credit for the first successful extrapleural ligation of a tracheoesophageal fistula with cervical esophagotomy, which he performed in stages from January 5 to March 27, 1940, after a preliminary gastrotomy. At almost the same time, Ladd⁵⁰ independently worked out an essentially identical procedure that was equally successful. According to Humphreys⁵¹ both these patients and several others operated on since that time by the same surgeons are still living at more than four years of age. With this plan of ligation of the fistula, esophagotomy and gastrotomy, an anterior thoracic esophagus is eventually constructed of skin by a series of plastic procedures, so that ultimately the patient conveys food and liquids from mouth to stomach by means of esophagodermatogastrotomy.

As stated above, the theoretical ideal is the establishment when possible of esophageal continuity by direct anastomosis. The first reported attempt was that made by Shaw⁵³ in 1939. Although the operation was successfully performed, a reaction from an elective transfusion resulted in death on the twelfth postoperative day. Haight and Townsley⁵⁴ report the first case successfully treated by extrapleural ligation of the tracheoesophageal fistula and end-to-end anastomosis of the esophagus.

In a recent personal communication, Dr. C. Haight states that he has been able to anastomose the two segments of the esophagus in 16 patients, 6 of whom are living; all of them have a patent esophagus. Five of these take all their feedings by mouth without difficulty, but in 1 case there is a high-grade stenosis for which retrograde dilatations are done from time to time. The sixth patient has a wide-open esophagus, but a recurrent tracheoesophageal fistula has been discovered. The oldest living patient was operated on three years ago and is doing extremely well. The youngest living patient has passed nine months since the operation.

Stricture

Simple severe stricture of the esophagus, the result of the ingestion of caustics or other severe cicatrizing trauma, has long been a discouraging problem. Frequent bouginage, a gastrotomy life or both are frequently the lot of these patients, many of whom are children or young adults otherwise in excellent health. Although the construction

*Assistant professor of thoracic surgery, Boston University School of Medicine; visiting surgeon in charge of thoracic surgery, Massachusetts Memorial Hospitals; visiting surgeon for thoracic surgery, Boston City Hospital.

if an anterior thoracic esophagus from skin has frequently been accomplished with satisfactory functional results, the method has many disadvantages. Not the least of these is the appearance of fistulas at the site of anastomosis of the skin tube with the cervical esophagus and especially with the stomach. Many ingenious technics have been devised, but the constant regurgitation of acid gastric contents into the skin tube of the reconstructed esophagus sets up an irritation that sometimes results in ulceration of the tube and formation of a fistula at the anastomosis. These fistulas are difficult to heal and therefore usually impede satisfactory reconstruction of the esophagus.

Recently Yudin,⁵⁵ director of surgery of the Sklifasovski Institute for Traumatic Diseases in Moscow, has reported on the surgical construction of an artificial esophagus in 80 cases. He recommends drawing a segment of jejunum through an anterothoracic subcutaneous tunnel as high as the angle of the left inferior maxilla, where it is immediately or at a subsequent stage anastomosed with the cervical esophagus. This author states that in his opinion a total intestinal plastic operation is the one of choice and is practicable in strictures located below the middle of the cervical section of the esophagus. The construction of the new esophagus should be carried out in two stages: exteriorization of the intestine—through a skin tunnel—up to the neck and direct anastomosis with the cervical esophagus. He believes that the operation should not be completed in one stage because of the tremendous risk of infecting the whole subcutaneous tunnel at the point of anastomosis of the esophagus and the jejunum. By July, 1943, Yudin had created artificial esophaguses in 88 cases, total intestinal esophagoplasties being performed in 21. The direct operative mortality was 2.3 per cent.

Carcinoma

In 1940, Garlock⁵⁶ wrote, "Heretofore, the diagnosis of carcinoma of the esophagus was tantamount to signing the patient's death warrant, and the physician advised palliative measures consisting of gastrostomy, radiation therapy or both." Because of the pioneer work and enthusiasm of this surgeon and many others, such a situation no longer obtains, and many probable cures have been accomplished in a disease that was once held to be beyond help and hope. The successful surgical resection of a cancer-bearing portion of the esophagus, particularly the lower and midportions, has been so frequently reported in the past five years that it may now be accepted as having passed beyond the stigma of a surgical stunt. It has been estimated that 5 per cent of all malignant disease occurs in the esophagus, with the proximal third involved in 18 per cent of these cases. Experience with radiation therapy

has given no encouragement, and surgery has afforded the only hope of a cure, so that the surgeon must do all in his power to establish an earlier diagnosis.

It has been customary to divide the esophagus into three parts, and to speak of the upper, middle and lower thirds. Churchill and Sweet⁵⁷ believe that it is more useful to divide it into fourths, the second and third fourths being thought of as the middle half. From the point of view of surgical management they consider three zones. Zone 1, the upper fourth, extends from the base of the neck to the superior surface of the aortic arch. Zone 2, the middle half, includes that portion extending from just above the aortic arch to just below the level of the inferior pulmonary veins. Zone 3 includes the lower fourth of the thoracic esophagus, the cardiac orifice of the stomach and the adjacent few centimeters of the stomach, as well as the fundus.

Carcinoma of upper esophagus (Zone 1). Bird⁵⁸ states that two factors appear to have contributed to the recent lack of interest in carcinoma of the upper third of the esophagus, as compared to the enthusiasm shown in the attack on growths in the middle and lower thirds. In the first place, the cases are not so frequent; secondly, the field of operation is ill defined, and the lesion most frequently encountered—Trotter's type of hypopharyngeal epithelioma occurring in young and middle-aged women—is prone to be neglected by both the laryngologist and the thoracic surgeon. Hudson⁵⁸ reports 2 cases of carcinoma of the proximal portion of the upper third of the esophagus that illustrate the value of complete removal of the lesion and the disappointment that may follow anything short of complete removal. The lesions are so intimately associated with the larynx or involve it in such a manner that both the esophagus and the larynx must be removed if a cure is to be expected.

The results of surgical excision in the upper esophagus have not on the whole been encouraging, but they are good enough to stimulate continued attempts at cure and perfection of technics. Radiation is only of palliative value.

Carcinoma of midesophagus (Zone 2). Approximately four fifths of the lesions in carcinoma of the esophagus occur in its thoracic and abdominal portions.⁵⁹ In general it may be said that the greater part of the thoracic esophagus must be removed if a carcinoma of the middle third is to be cured, and the Torek⁶⁰ operation or some modification of it has usually been employed. Up to 1939, the only certain cure of a carcinoma of the midesophagus was obtained in 1913 by Torek,⁶⁰ whose patient lived for twelve years after operation and died of pneumonia without recurrence, as shown at autopsy. There are undoubtedly others, since Garlock⁶¹ in 1941 stated that one of his patients was alive almost five years after resection. This operation entails preliminary gastrostomy and cervical

esophagostomy at the time of the transthoracic resection of the carcinoma, with the connection of these two stomas contemplated at a later date to re-establish continuity, usually by an anterior thoracic esophagus of skin.

There are many unsettled technical problems involved that need not be discussed in this review.

Churchill and Sweet⁵⁷ report 9 cases, with 3 patients alive and well. There were only 2 postoperative deaths. Ochsner and DeBailey⁵⁸ report 2 cases, with postoperative deaths in both. Phemister⁶² reports resection and cervical esophagostomy in 4 cases, with 3 survivals. Wu and Loucks⁶³ have operated on 4 patients with carcinoma of the midesophagus, with 2 survivals. Santy et al.⁶⁴ explored 6 patients and were able to resect the esophagus in 2, both of whom survived. Allison⁶⁵ describes 4 cases of esophageal carcinoma treated by the excision of the thoracic esophagus in 3 and of the stomach and abdominal esophagus in 1. All the patients survived the operation, but none lived longer than one year. Franklin⁶⁶ successfully removed the thoracic esophagus for cancer in 2 cases. One patient is well, and the other died thirteen months after operation. Carter⁶⁷ operated on 2 patients with carcinoma of the lower third by a modified Torek technic with 1 death in the hospital from meningitis and 1 recovery. Garlock⁶¹ has done 13 Torek or modified Torek operations with 6 deaths. One patient is alive almost five years later and another thirteen months later.

In a recent communication Garlock⁶⁸ states that he believes that greater mobility of the stomach can be obtained by dividing the branches of the left gastric artery so that the stomach can be pulled higher into the left pleural cavity without tension. He has also brought the proximal end of the esophagus anterior to the arch of the aorta and performed esophagogastrostomy in cases in which the Torek operation would formerly have been necessary. We have repeated this procedure at the Massachusetts Memorial Hospitals and have been gratified at the ease with which esophagogastrostomy can be performed with the aid of these maneuvers. It seems likely that continuity between the stomach and the esophagus can be established within the thorax in a greater number of middle-third (Zone 2) cancers by means of this technic than has hitherto been thought possible.

Carcinoma of lower esophagus and upper end of stomach (Zone 3). Carcinomas arising in the fundus or cardia of the stomach and extending to involve the lower esophagus pose an almost identical problem as do tumors arising in the lower esophagus itself, and operations on both types of lesions will be considered together.

According to Bird,⁴⁸ in spite of the fact that Biondi (1895), Sauerbruch in his early work and Janeway and Green (1910) had worked out an appar-

ently satisfactory endothoracic esophageal-gastric anastomosis on dogs and cadavers; no successful human cases were recorded until Ohsawa's in 1933.

At the 1938 meeting of the American Association for Thoracic Surgery, Adams and Phemister reported the first successful thoracic esophagogastrostomy for carcinoma performed outside of Japan. This was for squamous-cell carcinoma of the lower third of the esophagus. The resection followed careful preparation by experimental work on dogs and the authors had profited by experiences derived from a previous unsuccessful case.⁴⁸

Since that time, an increasing number of successful cases is being recorded in the literature. In 1940, Garlock⁶⁶ reported resection and esophagogastrostomy in 2 cases with 1 recovery. He also performed radical resection and intrathoracic esophagogastrostomy in 3 cases of carcinoma originating in the cardia, and stated that he was convinced that the only logical method of treating cancer in this situation was by the transthoracic transdiaphragmatic route. In the same year Carter et al.⁷⁰ reported 2 successful cases of transpleural esophagogastrostomy for carcinoma of the esophagus and for carcinoma of the cardiac portion of the stomach. Ochsner and DeBailey⁵⁹ have reported 2 cases, with 1 survival. Phemister⁶² states that resection and esophagogastrostomy were performed in 4 cases, in 2 of which carcinoma was primary in the esophagus and in 2 primary in the stomach. One patient in each group survived the operation. Wu and Loucks⁶³ have operated in this manner on 6 patients with carcinoma involving the stomach or esophagus or both, with 4 survivals. Garlock⁶¹ performed transthoracic resection with esophagogastrostomy for adenocarcinoma of the cardia and squamous-cell tumors of the distal esophagus. There were 15 cases with 6 deaths, an operative mortality of 40 per cent. Churchill and Sweet⁵⁷ report 11 cases in which resection and esophagogastric anastomosis for carcinoma of the stomach or lower esophagus was performed. There was 1 postoperative death, a mortality of only 9 per cent. Two of the survivors died of recurrent disease, but all the remainder were well and free from symptoms for from three months to two and a half years after operation.

Garlock,⁶¹ in summary, states that the general problem of the surgical treatment of cancer of the esophagus can, on the basis of his experience, be reduced to exact figures. The average patient with cancer of the middle third stands a 54 per cent chance of surviving the operation and a 30 per cent chance of living for over one year. With squamous-cell cancer of the distal third, the patient has a 70 per cent chance of surviving the operation and an almost 100 per cent one of living for over two years. In the group of adenocarcinoma of the cardia, the probability of operability is only 37

er cent; there is a 60 per cent chance of operative survival and an 80 per cent probability of living or over one year.

As may be noted from the foregoing reports, there has been a great advancement in the treatment of this disease by these methods. It is reasonable to expect even greater improvement in operability, mortality and survival with earlier diagnosis and greater experience in operative management.

THE THYMUS GLAND

There is no organ concerning which physicians have so little exact knowledge as the thymus gland. There has recently been some evidence of a relation between abnormalities of this gland and myasthenia gravis.⁷¹

Stimulated by the work of Blalock et al.,⁷³ who in 1941 reported the effects of removing the thymus gland from 6 patients with myasthenia gravis, the first concerted attack on this problem, Sloan⁷² examined 350 thymus glands. These included approximately 200 specimens removed during routine autopsies at the Johns Hopkins Hospital and 150 specimens removed from patients who died suddenly and were autopsied at the city morgue. Sloan's findings, in part, are as follows:

Examination of 10 thymus glands, none of which contained a tumor, removed at operation from patients with myasthenia gravis showed constant changes. In all there was some age involution and an increase in the number of lymphocytes present in the thymus. In 7 cases, abnormal numbers of lymphoid follicles with germinal centers were present in the medulla. There was no epithelial hyperplasia and no constant change in the character and number of Hassall's corpuscles. In 6 autopsied patients with myasthenia gravis who had not undergone operation there was no generalized lymphoid hyperplasia. The changes found in the thymus gland in myasthenia gravis were not part of such a generalized lymphoid hyperplasia.

Clagett and Root,⁷¹ reporting on 10 cases in which thymectomy was performed, with 1 death, state that their results have been satisfactory enough to warrant further employment of this operation in cases of myasthenia gravis and, at times, even in cases in which no thymic enlargement is demonstrable by x-ray. They discuss the advantages of the three approaches that they have used — transcostal, posterolateral and sternal splitting.

Hardy and Bradshaw⁷⁴ summarize the literature on the value of surgery in 132 cases of proved myasthenia gravis, including 3 of their own. Approximately 50 per cent have shown improvement. They believe that more cases must be operated on before conclusions can be drawn.

At the 1944 meeting of the American Association for Thoracic Surgery, Blalock⁷⁵ reported on the effects of thymectomy performed on 20 patients with severe myasthenia gravis. Only 2 of these

patients had tumors of the thymus. Approximately 8 showed striking improvement, whereas in the others there was only slight if any improvement.

Obviously much work remains to be accomplished on this fascinating subject. If a relation between the thymus gland and myasthenia gravis exists, there appears to be some factor that is not as yet understood.

THE HEART

In most cases of chronic heart disease, the physician is not able to effect a complete cure but is able to prolong life and to make the patient more comfortable. There are, however, some diseases of the heart or of the structures indirectly affecting it that respond brilliantly to surgical therapy. These conditions constitute only a small percentage of the total, but this does not minimize the importance of diagnosing and treating them (Blalock⁷⁶). It is with the surgical types of heart disease in which cure can often be effected that this review will be concerned.

Patent Ductus Arteriosus

The first attempt at obliteration of a patent ductus arteriosus was reported by Strieder⁷⁷ in 1937. The patient was operated on at the suggestion of Dr. Ashton Graybiel⁷⁸ and was already ill with subacute bacterial endarteritis. Death occurred on the fourth postoperative day and was due to acute dilatation of the stomach. The first successful case of surgical ligation of a patent ductus arteriosus was reported by Gross and Hubbard⁷⁹ in 1939. Since that time many successful cases have been reported, so that the operation has been established as a sound and rational procedure.

Burwell⁸⁰ has tentatively suggested the indications for the performance of this operation. These indications, which are generally accepted by most writers on this subject, are as follows: the presence of important limitation or actual heart failure, the demonstration that the patent ductus arteriosus is interfering with normal growth, or the presence of subacute bacterial endarteritis; and the demonstration of uncomplicated patency in itself, because of the probable utility of the operation in preventing progressive overwork of the heart and in preventing bacterial endarteritis in a young person. The latter constitutes a strong suggestion that operation should be considered.

In 1940, Jones, Dolley and Bullock⁸¹ reported the ligation of 13 cases, with 1 death. In 1942, Humphreys⁸² reported 16 cases, with no operative deaths. There was 1 late death from complications arising from the presence of a postoperative aneurysm of the ductus. Six patients were operated on because of subacute infection of the blood stream. Three of these were apparently cured, 1 was still in the postoperative period, 1 had died, and 1 still had positive blood cultures.

Touroff,⁸³ reporting on a series of 10 cases of patent ductus arteriosus complicated by infection, states that cures occurred in 7. There were 2 deaths from accidental hemorrhage and 1 failure ascribed to vegetations on the aortic valve. Thus, among 8 operative survivals there were 7 recoveries and 1 failure.

There have been many other reports of small series and single successful cases.

It seems likely that the operative mortality will be less than 10 per cent in the hands of experienced and skillful operators. Improvements in technic will undoubtedly lower this rate.

Gross⁸⁴ has recently described a carefully worked-out technic whereby in 14 cases he has successfully completely divided the ductus arteriosus. This, of course, is the method of choice, since it eliminates the possibility of recurrences by recanalization when the ductus has been treated by single or even double ligation.

Coarctation of Aorta

In an intriguing paper, Blalock and Park⁸⁵ describe 43 animal experiments during the course of which they divided the aorta below the arch and, turning down the left subclavian artery, anastomosed it with the distal portion of the aorta. There were 10 survivals of several months or longer. The authors suggest the possibility of using the common carotid artery in man to bridge a coarctation of the aorta, but believe that it should be considered only in human cases in which the outlook is very grave, since many patients with coarctation of the aorta have a fairly long life expectancy.

Trauma

In recent years there have been many reports of successful suture of penetrating wounds of the heart.⁸⁶⁻⁹⁶ One of the largest series is that of Bigger,⁸⁶ who operated on 17 patients at the Medical College of Virginia Hospital. Eleven recovered, and 6 died. Bigger also collected, by questionnaire, reports of 141 patients operated on by other surgeons and found that 71 recovered and 70 died, a recovery rate of approximately 50 per cent, which he believes more nearly approaches the actual recovery rate than do the figures collected from the literature. Elkin⁸⁷ reports 38 patients with heart wounds operated on by him or his resident staff. Of these, 22 recovered and none of them had any residual symptoms referable to the injury.

Blalock and Ravitch⁹⁶ discuss whether the total of successful end results would not be greater if a more conservative policy regarding immediate operation were adopted in cases in which there is no active bleeding through the chest wound or into the pleural cavity. To put the matter otherwise, may operation be delayed and aspiration of the pericardium be used in cases in which the symptoms are due to tamponade rather than to continued

active bleeding? Even if one decides to pursue this policy, facilities for immediate operation should be available and tamponade should not be allowed to persist for over two hours. If blood accumulates after aspiration, operation is indicated. This coincides with the following directions, recently prepared for medical officers in the United States Army relative to the treatment of penetrating heart wounds with resulting tamponade: aspirate the blood from the costoxiphoid route, if possible; repeat the aspiration if there is a recurrence; and if there is another recurrence, perform a cardiac raphy through an extrapleural exposure. Cases falling into this category, which have been or could have been treated conservatively, have been reported by Bigger,⁸⁶ Elkin⁸⁷ and Strieder.⁹⁷ It seems more likely, under these circumstances, that a coronary artery or vein has been wounded and the myocardium incised for only a portion of its thickness rather than that a complete penetration of the myocardium has occurred.

I have been asked by medical officers in the Army course in thoracic surgery how one can be sure, on performing pericardicentesis, that the aspirating needle is in the blood-filled pericardium and not in one of the heart chambers. This question is not so naïve as it might appear at first glance, since I have seen blood aspirated directly from the heart of unsuspectedly large proportions with the operator under the impression that he was aspirating a hemopericardium, which actually was not present. As in any procedure, one gains facility only with experience, but if the needle is advanced slowly by the costoxiphoid route, a definite sensation is transmitted to the operator as the pericardium is perforated and at this point blood is obtained once as the plunger is withdrawn. If the needle is cautiously advanced a short distance farther, the movements of the heart can be felt against the tip of the needle, which should then be withdrawn to the original depth at which blood was first obtained.

It seems, however, that not operating on a patient with a wound of the heart is an extremely hazardous course to follow. Nelson⁹⁸ believes that in all cases of penetrating thoracic wounds in which it cannot be determined positively that the wound has not reached the heart should have exploration performed.

Olim and Hughes⁸⁸ and Zerbini⁸⁹ have each reported a case in which it was necessary to ligate the left anterior descending coronary vessels to repair stab wounds of the right ventricle. Both patients recovered, and follow-up indicated that they were unaffected by the procedure.

Nonpenetrating wounds of the heart resulting in contusion and rupture have been discussed by Elkin,⁸⁷ Bright and Beck,⁹⁹ Beck,¹⁰⁰ Leinoff¹⁰¹ and Barber.¹⁰² These authors agree that this type of injury is a frequent, though often overlooked, cause

of death. Compression of the heart between the sternum and the bodies of the vertebrae, as when a driver is thrown against the steering wheel in an automobile collision, is a frequent mechanism resulting in cardiac contusion or rupture. Bright and Beck⁹⁹ analyzed 152 cases in which death was caused by rupture of the heart, as shown by autopsy. They conclude that an accurate differential diagnosis between cardiac contusion and coronary disease is almost impossible. On the other hand if a patient who has previously been in good health receives an injury and develops signs of circulatory embarrassment, he should be considered as having sustained cardiac injury. Treatment consists in absolute rest and sedation, mild laxatives to avoid straining and digitalis as necessary for irregularities. Rupture, if it is not an immediately fatal lesion at the time of injury, ordinarily occurs in the second week. Immediate operation is indicated, hence a thoracic surgeon should be readily available during this period. The authors suggest a pericardial graft at the suture line if the myocardium is infiltrated or extensively bruised or softened.

Crynes and Hunter¹⁰³ believe that the supposed rarity of traumatic rupture of the pericardium is not correct. They think that the scarcity of information concerning pericardial rupture is probably due to the fact that it is usually but one of multiple injuries terminating fatally and in itself may or may not contribute to the cause of death. They discuss a case in which was discovered an extensive pericardial rent, occurring in the absence of evidence of serious damage to the thoracic or abdominal viscera. The patient, a boy, lived for two and a half years after a crushing injury with but few symptoms attributable to the lesion present at autopsy.

Decker¹⁰⁴ raises the question whether foreign bodies in the heart and pericardium should be removed. He reviews 109 cases of foreign bodies in heart and pericardium reported since 1900, and states that foreign bodies should not be removed simply because of their presence. No emergency exists in those patients who survive the original trauma, unless one chooses to consider that free bodies in the pericardial cavity, sharp needlelike bodies and large objects need immediate or early surgery. Indications for removal must be based on prognosis and review of the condition of the patient and the degree and duration of the disability.

Turner¹⁰⁵ reports a case in which a bullet, with its base in the myocardium, protruded into the chamber of the left ventricle. When the heart was exposed at the time of the original injury, the bullet could not be seen or palpated and the attempt to remove it was reluctantly abandoned. The patient was well twenty-three years later.

Suppurative Pericarditis

Suppurative pericarditis is not a rare disease, but it must be suspected and sought in cases of generalized or thoracic infection if the diagnosis is to be made in a high percentage of cases. Strieder and Sandusky¹⁰⁶ reviewed 28 cases collected from the literature from January 1, 1934, to January 1, 1940, and added 10 cases from the Boston City Hospital, which brought the total of the recorded cases for which pericardiostomy had been performed to 265. The mortality for cases so treated is approximately 50 per cent. Without operation the mortality approaches 100 per cent. With the advent of chemotherapy the mortality with operation should be further reduced. When the diagnosis is made, operation should be undertaken forthwith. There is no reason for delay as there is in early empyema thoracis. It is unfortunate that some physicians are under the impression that chemotherapy together with pericardicentesis suffices to effect a cure in a large percentage of cases. If chemotherapy is of value as an adjunct, its effectiveness should be measurably increased by the prompt establishment of early, open, adequate pericardiostomy.

In cases with generalized infection, even with pericardiostomy, the prognosis remains that of the pre-existing infection, although, by relief of the cardiac tamponade, the operation may be a life-saving measure. Adams and Polderman¹⁰⁷ performed pericardiostomy on 3 patients with pneumococcal pericarditis, 1 of whom recovered. Of the 20 cases reported by these authors, 12 were secondary to pneumonitis or pneumonia, 6 to osteomyelitis, 1 to cholecystitis, and 1 to mastoiditis. In 5 patients with staphylococcal pericarditis an abscess was found in the heart muscle. The electrocardiogram may be of diagnostic aid in such patients. Malec and Midelfart¹⁰⁸ successfully performed pericardiostomy in a case of purulent pericarditis complicating streptococcal empyema. They advocate early adequate drainage and state that it rarely results in postoperative adhesive pericarditis, an opinion that is shared by Shipley.¹⁰⁹ In an operative experience with 8 cases, with 4 recoveries, I have not observed adhesive pericarditis as a late complication.

For purulent pericarditis the low anterior approach with the resection of the fourth and fifth left costal cartilages is probably the best, and is the one oftenest used. Donaldson¹¹⁰ has recently advocated a modification of the old Allingham approach for the drainage of nonpurulent effusions.

Constrictive Pericarditis

Since Churchill's¹¹¹ report in 1929 of the first successful resection of the pericardium for con-

strictive pericarditis in the United States, many other successes have been recorded, and the operation is now the accepted treatment in suitable cases of this disease. Blalock and Burwell¹¹² have published an important review of the subject, to which the reader is referred. In it they discuss 28 cases of constrictive pericarditis that they observed at the Vanderbilt Hospital in Nashville, Tennessee. The etiologic agent was established in 21 cases by aspiration, operation or autopsy, and was found to be the tubercle bacillus in 18 cases and *Staphylococcus aureus* in 3. Twenty patients had pericardectomy. Twelve were cured or greatly improved, whereas 8 died from several hours to two years after operation. These results are in accord with previous observations that approximately 60 per cent of the patients are either cured or greatly improved by the operation.

Harrington and Barnes¹¹³ discuss the diagnosis and surgical treatment of chronic constrictive pericarditis and report 9 cases. Three patients were cured, 3 were improved, and 3 died, the deaths occurring three, four and twenty-nine days, respectively, after operation. Heuer and Stewart¹¹⁴ have reported 7 operations without a death. Three of the patients were cured and 4 were markedly improved.

Tumors

Gebauer¹¹⁵ reports a case of a huge intrapericardial teratoma containing a large, probably infected dermoid cyst that he removed at operation from a twelve-year-old girl. The patient died of uncontrolled hemorrhage from the aorta, which was inadvertently injured.

Beck¹¹⁶ has successfully removed an intrapericardial teratoma. He also describes a case of a tumorlike mass in the wall of the left ventricle. The identity of the lesion was not established, but it was probably not a true neoplasm. This seems to be the first case in which a benign lesion of the heart has been recognized clinically and the only one in which removal of the lesion has been effected surgically. The patient was in good condition eighteen months after operation. Aneurysm of the left ventricle had not developed.

Angina Pectoris

Attempts to improve the blood supply to the ischemic heart by the establishment of a collateral circulation by surgical measures have continued. Unlike total thyroidectomy and alcohol injections about, or operations on, the sympathetic cord and rami of the upper thoracic region, which treat only the symptoms of angina, these attempts are based on physiologic principles and are directed at the underlying disease.

Beck¹¹⁷ was the first surgeon to apply these principles. His original operation consisted in grafting the pedicled pectoralis major muscle to the heart.

Schildt et al.,¹¹⁸ experimenting on dogs to produce new communications between the coronary arteries by the application of inflammatory agents to the surface of the heart, found that powdered asbestos was the most satisfactory substance. It reduced the mortality and the size of the infarct following ligation of a coronary artery. Recently, Beck¹¹⁹ has utilized this work and describes a new operation in which he abrades the parietal pericardium with special burrs and introduces powdered asbestos to further adhesions between the heart and mediastinal fat. He believes that fat is probably the best tissue for purposes of vascularization, but that all tissues that come in contact with the heart serve as grafts.

Feil¹²⁰ appraises the results in 37 patients with sclerosis of the coronary artery and angina pectoris operated on by the Beck technic. There were 14 postoperative deaths, a mortality rate of 38 per cent. Nine patients survived the operation but died four months to six years later. In 5 of these cases the results were excellent, and in 4 there was little or no improvement. Fourteen were still living, and of these, nine were definitely improved and 5 showed an increase in exercise tolerance and diminution in symptoms. The results in the 23 patients who survived the operation were as follows: excellent, 14 cases (61 per cent); good, 5 (22 per cent); little or no improvement, 4 (17 per cent).

O'Shaughnessy,¹²¹ of London, whose brilliant work was terminated by his death in Flanders before Dunkirk while serving with the British Army, used the omentum as a vascularizing agent in an attempt to increase the circulation to the heart. He reported his results in 20 cases. Fifteen of these patients were suffering from angina pectoris; 5 of these died and 8 of the remaining 10 were free of angina, 7 having returned to work.

Strieder and Clute¹²² have operated on two patients using the O'Shaughnessy technic. In one case there was an excellent result, but death occurred six months after operation as a result of an operation for diaphragmatic hernia, which was a complication of the original cardio-omentopexy. The second patient was still alive four years later, with only slight improvement in the angina but with a greatly increased exercise tolerance.

Thompson and Raisbeck¹²³ found that in animals adhesive pericarditis can be regularly produced by the introduction of sterile talc into the pericardial sac. Ligation of the descending ramus of the left coronary artery and vein at a point 1 cm. below the origin of this artery carried a mortality of 50 per cent. If this operation was repeated but in addition talc was introduced, the mortality was 25 per cent. In another group, talc was introduced and two or three weeks later a similar ligation of the artery was performed. In this group there were no deaths. Beck¹¹⁹ repeated these experiments but was unable to obtain the same bene-

ficial results as these authors report. Thompson and Raisbeck have, however, reported gratifying results in a group of patients incapacitated by their angina, who were completely or partially relieved of pain and were able to return to work.

I have introduced aleuronat paste into the pericardium of a woman who was completely incapacitated by angina pectoris. She is alive and doing her own housework four years later. Another patient, a man suffering from angina pectoris secondary to syphilitic aortitis, has been treated by introducing talc into the pericardium. At the time of operation he was unable to walk the length of the ward without precipitating an attack, but one year later he was able to walk four miles without pain. He died in cardiac failure one year after operation, and autopsy showed complete obliteration of the pericardial space with a rich collateral vascular system.

A somewhat different approach to this problem has been used by Fauteux,¹²⁴ who found that if he ligated the magna cordis vein of the dog's heart and ligated the descending ramus of the left coronary artery, the mortality was much less than if he ligated only the artery. The important practical result of this procedure was a rise in arterial pressure in the entire apical region of the heart, the area drained by the surgically occluded vein. Fauteux and Palmer¹²⁵ ligated the great cardiac vein in 6 patients. One, a man of fifty-four, was working as a janitor two years after the intervention. Five others survived the operation for shorter periods of time. All were relieved of pain.

There is no implication that ligation of a vein will prevent thrombosis in an atheromatous but patent coronary artery, but there is evidence that venous ligation will cause changes in the vascular bed, such that, if thrombosis does subsequently occur, infarcts may be limited in size if not actually prevented from forming.

This highly important and controversial subject is still in a state of flux, and much work remains to be done. Many more patients must be operated on and the results must be carefully appraised before significant conclusions can be drawn. Beck¹²⁶ best sums up the matter as follows:

Our interest should be focused on the point as to whether or not a reasonable quantity of blood can be made to pass from the grafts into the heart, regardless of the procedure and regardless of the tissue used . . . We have been able to demonstrate vessels between the grafts and the heart, however, we have no way of knowing how much blood went through these channels. If these channels are numerous enough and large enough to transport a reasonable quantity of blood, then the principle upon which the operation is based would be established. If the principle were satisfactorily established, then the best method for doing the operation would become important.

Intracardiac Surgery

Harken¹²⁷ believes that recent advances in thoracic surgery suggest that it is time to take up experi-

mental intracardiac surgery. Working in the surgical research laboratories of the Boston City Hospital, he has devised an ingenious method of producing bacterial endocarditis by attaching a metal clip to the posterior mitral leaflet. The clip is introduced through the left auricular appendage. Following the injury to the valve leaflet, the character of the endocarditis and the specific nature of the vegetations were directed by the administration of sulfanilamide derivatives and subsequent injection of the desired bacterial strains. Harken¹²⁸ has also devised a new cardioscope by means of which it is possible to visualize in the experimental animal the chambers of the heart, the valve leaflets, the clips in place and the chordae tendineae with moderate facility. It is entirely within the realm of speculation that some day cardioscopy will play an important part in surgery of the heart.

171 Bay State Road

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 30371

PRESENTATION OF CASE

A thirty-three-year-old bartender was admitted to the hospital because of jaundice.

The patient was apparently well until about six weeks prior to admission, at which time he noted that he tired easily and lacked his usual vigor. His appetite became poor, and he had episodes of morning nausea and vomiting. He also developed muscle cramps in the legs, low backache and brief cramplike epigastric pains just to the left of the midline. Two and a half weeks before entry he was told that the whites of his eyes were becoming yellow, and this was followed in a few days by a noticeable yellowing of the skin, which continued to increase. There was no associated pruritus, and there was no history of chills or fever. The urine became dark, but the stools remained normal in color. Frequent doses of magnesium citrate were taken for constipation. A few days prior to entry he noticed that the abdomen was enlarging and felt firm. On the day of admission a small amount of bright-red blood was noted in the stools.

For the preceding ten years the patient had been a bartender and was in the habit of drinking about a pint of liquor, supplemented with ten to twelve glasses of beer or ale, daily. He often went without food for several days at a time, although consuming the usual amount of alcohol. He smoked heavily — two or three packages of cigarettes daily — but denied taking drugs. There was no history of intolerance to fatty foods, abdominal distress or previous attacks of jaundice. The patient had noticed occasional swelling of the ankles in recent months.

The family history revealed that his mother had been operated on for gallstones and that his father, also a heavy drinker, had been confined at a state hospital for several years.

Physical examination on admission revealed a well-developed rather obese man who was intensely jaundiced. The skin was lemon yellow rather than orange or bronze. A few small spider angiomas were present on the anterior chest and right upper arm. The palms of the hands were erythematous, especially at the periphery. The tongue was beefy

*On leave of absence.

red and slightly smooth. The heart and lungs were clear. The abdomen was moderately distended. The liver edge was tender and palpable a hand-breadth below the costal margin and also to the left of the midline. The knee and ankle jerks were absent, and there was hypoactivity of the deep tendon reflexes of the upper extremities. The calves were tender to pressure.

The temperature was 100.4°F., the pulse 88, and the respirations 24. The blood pressure was 100 systolic, 65 diastolic.

Examination of the blood revealed a red-cell count of 3,490,000, with 12.5 gm. of hemoglobin. The white-cell count was 11,700, with 85 per cent neutrophils. The urine had a specific gravity of 1.010 to 1.020, with negative to ++ tests for albumin and a ++++ test for bile. The sediment on one occasion revealed numerous bile-stained coarsely granular casts; no leucine or tyrosine crystals were seen. The urine urobilinogen varied from negative to positive in a 1:16 dilution. Although one clay-colored stool was seen on admission, subsequent specimens were brown, soft and formed, often with a positive guaiac test. The van den Bergh test was 8.0 mg. direct and 22.0 mg. indirect. The serum protein was 5.7 gm. per 100 cc., with an albumin-globulin ratio of 1.0. The cephalin-flocculation test was + in twenty-four and ++ in forty-eight hours. The alkaline phosphatase was 5.0 Bodansky units per 100 cc. The nonprotein nitrogen was 33 mg. per 100 cc., and the cholesterol 134 mg. The prothrombin time was 38 seconds (normal, 18 to 20 seconds). A blood Hinton test was negative.

Roentgenographic examination of the abdomen revealed no evidence of stones, but there was definite enlargement of the liver and spleen. The patient was treated with transfusions, dextrose and Amigen intravenously and vitamins and choline by mouth. He had one transfusion reaction. His temperature varied between 100 and 102°F., with morning remissions.

On the tenth hospital day the spleen was palpable, and in the following days the spleen became larger while the liver appeared to diminish in size and to become more tender. Definite ascites was demonstrable. The van den Bergh was now 12.4 mg. direct and 18.0 mg. indirect. The nonprotein nitrogen rose to 47 mg. per 100 cc., and the serum protein fell to 4.7 gm. The cephalin-flocculation test was + in twenty-four and ++ in forty-eight hours. The chloride was 86 milliequiv. per liter. The fasting blood sugar was 110 mg. per 100 cc. before and 117 mg. after the administration of 0.7 cc. of a 1:1000 adrenalin solution.

The patient continued to vomit and to complain of epigastric pain. Several stools contained gross blood, and on the sixteenth hospital day a clay-colored stool was noted. He became semicomatose and died on the nineteenth hospital day.

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PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this patient showed, as was expected, a good deal of ascitic fluid. The spleen was quite enlarged, weighing 450 gm. The liver presented an unusual appearance. It was large, weighing 3500 gm., which is about two and a half times the normal size, and was olive green and moderately firm; scattered throughout the organ were several small, finely nodular areas, averaging 1 to 3 mm. in diameter. The large size of the liver, plus the fact that it was green, made one believe that this was an obstructive cirrhosis. It had all the gross characteristics of obstructive cirrhosis or a biliary cirrhosis, except that the bile ducts were perfectly normal in caliber and there was no evidence of extrahepatic biliary obstruction. At the time of autopsy we toyed with the idea that this might have been one of the rare cases of intrahepatic cholangitic biliary cirrhosis. Microscopic examination, however, showed that the gross observations were incorrect, and that the diagnosis was alcoholic cirrhosis. Almost every other cell contained the characteristic alcoholic hyalin that is seen in the degenerated liver cells, and there was a fair amount of fat scattered throughout. There was early connective-tissue formation, but not the dense fibrous tissue that one sees in longstanding cirrhosis. In other words this is what has been called a "subacute alcoholic cirrhosis,"* a liver on its way to the chronic stage. Perhaps a year before it weighed about 5000 gm., was full of fat and had little, if any, connective tissue; at the time of death it was beginning to shrink. There was a great deal of necrosis in the liver cells, with polymorphonuclear and lymphocytic infiltration, which one could argue was either an acute hepatitis or a toxic manifestation from whatever produces alcoholic cirrhosis. In any event acute degeneration was still going on.

There were many purpuric spots throughout the lung and slight focal bronchopneumonia. The kidneys were tremendous in size, each weighing almost 400 gm., and microscopically showed a bile nephrosis. The heart weighed 400 gm. and was markedly dilated, which possibly was a manifestation of vitamin deficiency.

CASE 30372

PRESENTATION OF CASE

A sixty-nine-year-old Norwegian housewife was admitted to the hospital because of pain in the epigastrium.

As a result of the patient's poor memory the history obtained was rather inadequate. Fifteen years prior to admission she underwent an abdominal

operation but was unable to state what had been done. Since that time pressure sensations and pain in the epigastrium had become increasingly frequent after meals, especially after the ingestion of greasy foods, fruit and desserts. Nine months prior to entry she noted increasing tiredness, associated with dyspnea on exertion and orthopnea. On consulting a physician, she was told that she had heart disease, and she was treated with digitalis and bed rest on and off for a period of three months, with apparent improvement. Three weeks before admission she developed severe epigastric pain after eating liver. The pain persisted and interfered with sleep, and she became increasingly weak, so that hospitalization was advised. She had lost about 20 pounds over a period of two or three years.

Physical examination on admission revealed an emaciated woman with a sallow complexion. Bilateral lens opacities were present. The pulse was flatly irregular, and cardiac murmurs were audible. Palpation high in the left upper quadrant revealed tenderness and a fullness that suggested a mass.

The blood pressure was 135 systolic, 90 diastolic. The temperature was 99°F., the pulse 90, and the respirations 20.

Examination of the blood revealed 13.8 gm. of hemoglobin and a white-cell count of 15,600, with 84 per cent neutrophils. The urine had a specific gravity of 1.020 and gave a + test for albumin; the sediment contained 4 red cells, 6 white cells and many epithelial cells per high-power field. The blood nonprotein nitrogen and sugar were normal. The serum protein was 6.1 gm. per 100 cc., and the chloride 94 milliequiv. per liter. A Hinton test was negative.

A gastrointestinal series revealed no intrinsic esophageal gastric or duodenal lesion. A mass was visible in the midabdomen, medial to the body of the stomach and tending to displace it to the left. No adhesions between the stomach and the mass could be demonstrated.

On the fourteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL C. MILLER: The history and physical examination in this case are rather incomplete. We have no data that allow the pathology to be attributed to any one system of the body, except perhaps for two or three apparently minor details. The patient was an old woman who had apparently been going downhill for fifteen years, although the weight loss and indigestion were more marked during the two or three years prior to admission. It seems to me that we have to rule out certain conditions of the gastrointestinal and urinary tracts before going to the other systems and organs that might be involved. There was one x-ray study, a gastrointestinal series. May we see the films? I think that the description is clear enough in the record,

*Hall, E. M., and Morgan, W. A. Progressive alcoholic cirrhosis: clinical and pathological study of sixty-eight cases. *Arch. Path.* 27: 672-690, 1939.

DIFFERENTIAL DIAGNOSIS

DR. FRIEDRICH W. KLEMPERER: This is, in brief, the story of a thirty-three-year-old man who for ten years had lived on alcohol and inadequate food. Then, without obvious reason, he proceeded suddenly, within two months, from good health to a death due to dysfunction of the liver. Practically all the symptoms, physical signs and laboratory data can be explained by dysfunction of the liver and avitaminosis. He had a short prodromal period—three and a half weeks—of vague complaints. He then became increasingly jaundiced and constipated and the liver began to enlarge. We do not know whether the liver had been large before this episode. He had had swelling of the ankles for several months. This is hard to interpret. It may have been due to cirrhosis of the liver. It could, however, be adequately explained on the basis of avitaminosis and protein deficiency. We know that the serum protein was low. It may also have been on a cardiac basis, because a beri-beri heart is frequently seen in alcoholic addicts.

On admission he was intensely jaundiced and the skin was lemon yellow rather than orange or bronze. We know that the urine contained bile, and the lemon-yellow color is therefore explained by the combination of bilirubin jaundice and anemia. Spider angiomas are typical of liver disease. "The tongue was beefy red and slightly smooth." This represents evidence of niacin (nicotinic acid) deficiency. We also have evidence of thiamine deficiency, because he had absent knee and ankle jerks and hypoaactive deep tendon reflexes of the upper extremities. The anemia may have been on a deficiency basis or may have been caused by blood loss from the intestinal tract. This bleeding could be adequately explained by the prolonged prothrombin time, again a sign of dysfunction of the liver. The renal function was good, as judged by the specific gravity of 1.020. Slight albuminuria was present, as often occurs in cases with marked damage to the liver. Bile was excreted in the urine, and also a small amount of urobilinogen, which indicates that bile passed into the intestine. The van den Bergh test gave high values, particularly by the indirect method, which is usually taken as an indication of damage to the liver cells and is evidence against an obstructive jaundice. We have further laboratory evidence of liver dysfunction in the low serum protein, particularly the low albumin, the positive cephalin-flocculation test, the prolonged prothrombin time and the decreased cholesterol. The adrenalin-glucose test simply means that there was not enough glycogen in the liver to be broken down to give a significant rise in blood sugar.

From the time of admission the course was gradually downhill, and the patient died the usual death of liver insufficiency.

The cause of this man's liver deficiency was most probably a combination of avitaminosis, protein-deficiency and alcoholism. A primary infectious disease, such as Weil's disease, can safely be ruled out because of the long afebrile prodromal period and the absence of nephritis. We are told that the patient had not taken any drugs, so that a toxic hepatitis due to something other than alcohol can probably be ruled out. There is one other possibility that I do not believe can be ruled out clinically and certainly not pathologically; that is, the hypothetical virus that causes so-called "catarrhal jaundice" may be superimposed on liver damage already done by the alcoholism and in this way cause a rapid downhill course. We have some clinical evidence against it—the relative length of the prodromal period and the absence of leukopenia and lymphocytosis. Because I know that the pathologist cannot tell this kind of jaundice from toxic hepatitis, I feel safe in ruling it out.

The question remains, Did the patient have cirrhosis of the liver or subacute yellow atrophy, that is, degeneration of the parenchyma of the liver? The course to my mind is somewhat too rapid for cirrhosis of the liver. The absence of evidence of collateral circulation does not help in differentiating the two conditions, because it hardly would have developed within two months. Ascites was not a predominating symptom, except toward the end of the disease. I cannot rule out a cirrhosis of the liver that was asymptomatic previous to the terminal episode, but there is no evidence in the record to support this view. I believe that, as occasionally is seen in alcoholism, the patient died of parenchymatous degeneration of the liver with fatty degeneration. Two months are enough time to give rise to regeneration and fibrotic changes in the liver, so that cirrhosis or beginning cirrhosis may also have been seen at autopsy.

CLINICAL DIAGNOSES

Subacute yellow atrophy of liver, with hepatic failure.
Alcoholic cirrhosis, early.
Splenomegaly.
Ascites.

DR. KLEMPERER'S DIAGNOSIS

Toxic alcoholic hepatitis, with early cirrhosis.

ANATOMICAL DIAGNOSES

Subacute alcoholic cirrhosis of liver.
Ascites.
Jaundice.
Hemorrhages into lung parenchyma.
Bile nephrosis.
Bronchopneumonia.
Cardiac dilatation.

iller was not much smarter than we were. When this woman came in she was miserable, as well as rattling, as it states in the record. We thought she had a carcinoma of the pancreas. I did not want to operate, but the family doctor, who was younger than we were, thought she ought to be operated on. I doubted that we could do more than establish a diagnosis.

CLINICAL DIAGNOSIS

Carcinoma of pancreas.

DR. MILLER'S DIAGNOSIS

Pancreatic cyst?

Retroperitoneal malignant tumor?

Hepatoma?

ANATOMICAL DIAGNOSES

Cholelithiasis.

Chronic cholecystitis.

Choledocholithiasis.

Chronic passive congestion of liver.

Anomalous lobe of liver?

PATHOLOGICAL DISCUSSION

DR. McKITTRICK: At operation the mass proved to be a congested liver. In retrospect, we paid too little attention to the fibrillation and to the pos-

sibility that it might have led to cardiac decompensation and an enlarged liver, thus accounting for the mass; in other words, we "missed the boat." But that was not all. What she really had was a gall bladder full of stones and a common duct full of stones, which are what the family doctor suspected. So through a left-sided incision we took out the gall bladder and removed the stones from the common duct. Then, thanks to the help of Dr. Conger Williams of the Cardiac Department, her heart failure was properly treated and she was not much the worse for wear. Of course we were extremely anxious to get her well after we had learned that she did not have cancer of the pancreas.

DR. CASTLEMAN: The biopsy of the liver showed slight congestion, not severe failure, and I wonder if the mass was merely an anomalous lobe.

DR. McKITTRICK: As a matter of fact, the patient had clinical heart failure, but some of us did not recognize it.

DR. CASTLEMAN: The gall bladder showed marked inflammatory change.

DR. McKITTRICK: This case provides one good lesson: one has to be very careful about getting the mind centered on a particular thing. Dr. Miller and I both centered our minds on the mass.

but it will be interesting to see the exact location of the tumor mass.

DR. LAURENCE L. ROBBINS: I should be glad to talk about the tumor mass but I cannot see it; the statement in the record was probably based on an observation made during fluoroscopy. The body of the stomach is more to the left than usual, but I certainly cannot see anything that suggests a definite mass pressing against the stomach.

DR. MILLER: Was a pyelogram made?

DR. ROBBINS: No. I think that I can see the upper pole of the right kidney, which looks all right. This may be the left kidney. Since the films were not taken with that in mind, it is difficult to be sure about them.

DR. MILLER: Except for a possible connection with the stomach, an x-ray study such as this would probably be of significance only in localizing the tumor more accurately. Were any guaiac tests on the stools reported?

DR. BENJAMIN CASTLEMAN: No.

DR. MILLER: And no diastase or amylase tests?

DR. CASTLEMAN: No.

DR. MILLER: It seems to me that the discussion must come down in a rather vague way to two questions. What tumors occur in the left upper quadrant? What is the likeliest diagnosis in this particular case?

From the description of the x-ray films and the fluoroscopic examination, I suspect that the tumor was not in the splenic area. A kidney tumor, possibly a large cyst or a hypernephroma, may displace other viscera one way or another. The fact that there was no connection between the tumor and the stomach rules out fairly well a lesion in the stomach. The gall bladder is a curious organ in that it may, when enlarged, extend in a number of directions. Usually hydrops of the gall bladder extends downward and a mass may be found in the right lower quadrant, but it is unlikely to extend to the left in the region of the lesser curvature of the stomach. The retroperitoneal region must also be considered. The retroperitoneal tumors most generally found in this location are the fibrosarcomas and lymphomas. Then there are mesenteric cysts in the gastrohepatic and gastrocolic ligaments. Mesenteric cysts are most frequently found in young children and extremely rare in the sixty-nine-year-old range. The pancreas is the next likeliest, perhaps I should say the likeliest, location for a tumor that presents in the region of the lesser curvature of the stomach. Pancreatic cysts are fairly frequent and are usually not associated with any changes in blood chemistry, digestive processes or other physiologic reactions. They gradually increase in size, displace organs and finally become diagnosable either by palpation or because of pressure symptoms on adjacent organs.

Another diagnosis that is interesting to postulate is a tumor of the left lobe of the liver, such as a

hepatoma. I have seen one such case in which the hepatoma presented by x-ray as a solid mass in the left upper quadrant medial to the stomach.

Are there any data in the history that lead us to a diagnosis of any one of these conditions? The first symptoms were pressure and pain. Naturally with a tumor of increasing size there might have been a sense of pressure, particularly after eating. As the stomach became filled with food there were symptoms of indigestion, particularly after greasy foods, fruits and desserts, which are more poorly digested than other foods. This could have been due simply to pressure against normal peristalsis. The suggestion of greasy food makes one think of a disorder of the gall bladder, liver or pancreas, but I do not believe that we have enough evidence of disease in either of these organs to be incriminating except perhaps for the pancreas, as I have said.

The pressure and pain were experienced intermittently and progressively over a fairly long period of time — three weeks before she was admitted. What is it in tumors and cysts that causes trouble? If the cyst has a pedicle it may become twisted and thereby infarcted. Its enlargement may cause pain owing to stretching of the capsule, and if it enlarges so as to press on its own mesentery it will cause various changes incident to gangrene or infarction. Infection is also a frequent complication of cysts. This again causes swelling and infarction if the process goes on long enough. The other eventuality is the development of malignant degeneration.

The laboratory data provide no significant information. The patient had a temperature of 99°F — a bare elevation — and a white-cell count of 15,500, with 84 per cent neutrophils. This would go along with hemorrhage or with the early stages of infarction of a tumor. We do not know whether the urine was a catheter specimen. It gave a + test for albumin, and the sediment contained 4 red cells. If it was a catheter specimen, the presence of the red cells is important. A woman of this age may have senile vaginitis, with red cells in a voided specimen; if it was a catheter specimen, however, the red cells probably came from higher up. There is no other sign of involvement of the kidney, but the failure to take an intravenous pyelogram resulted in the missing of an opportunity to see a tumor. The blood sugar was normal. In pancreatic cysts there is often not enough damage to the pancreatic substance to produce a diabetic state or any change in the amylase or diastase level. The blood protein was normal, and the chloride slightly depressed.

My first diagnosis, a purely presumptive one, is pancreatic cyst. The next two possibilities, which are less likely, are a retroperitoneal solid tumor with malignant degeneration and a hepatoma.

DR. LELAND S. MCKITTRICK: I am not proud to carry on this discussion, and I am glad that Dr.

rhythm may result.^{9,10} The observations of Winkler, Hoff and Smith,¹¹ however, indicate that the chief objection to the use of potassium salts arises from their possible irritating effect on the upper gastrointestinal tract. This irritation is probably of significance when potassium chloride or iodide is used, but probably is less important when potassium bicarbonate, acetate or citrate is employed. The findings of these workers indicate that serious cardiac complications or fatal poisoning from the oral administration of potassium is a distinct possibility only when there is complete, or almost complete, anuria associated with a high degree of nitrogen retention. They state, "The relatively slow absorption, the vomiting when large doses are given, the mode of distribution in the body and, most important of all, the continued ability of the most severely damaged nephritic kidney to excrete potassium all combine to make such poisoning very difficult to bring about."

The use of potassium bicarbonate, or that of the acetate or citrate if either is readily available, thus offers a useful adjunct to sulfonamide therapy and is certainly worthy of extensive clinical trial. Until more information concerning toxicity becomes available, it seems advisable to use small doses (5 to 10 gm. daily) and to administer these substances with care to nephritic patients who show evidence of moderate or marked nitrogen retention.

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QUALITY VERSUS QUANTITY PRODUCTION

THE Maternity Center Association of New York, in the June issue of its bimonthly broadside *Briefs*, points out the advances that have been made in reducing maternal and infant mortality, as well as some of the dangers that continue to exist. Despite the difficulties imposed by war conditions, with shortages of physicians and nurses and overcrowding of hospitals, the maternal mortality in the United States reached a record low level of 2.1 per 1000 live births in 1943. Infant mortality also achieved a new low point.

This success is attributed to the following factors: the profit derived from studies of the causes of maternal mortality; public education; advances in obstetric knowledge, with new, important life-saving discoveries; the increasing rate of hospitalization; the Social Security Act, with the Government entering the field of maternity and infancy care on a grand scale; and the Emergency Maternity and Infancy Care Plan for the wives of men in the four lowest pay grades of the armed services.

Dangers that still block our arrival at a millennium are listed as follows: the continued existence of many poorly managed and poorly equipped small hospitals in both urban and rural areas; the continued high death rate of infants under one day of age, due largely to prematurity and birth injury; continued outbreaks of infectious diarrhea of the newborn; and lack of positive good health and hygienic living conditions for so many of our expectant mothers.

From the expansion of this theme—the reduction in maternal and infant mortality—the broadside goes on to a somewhat ambiguous discussion of the political aspects of birth rates. In this discussion the usual failure to distinguish properly between quality and quantity production is found. All political leaders, mindful mainly of muscular competition between nations, have viewed declining birth rates with apprehension and have rightly feared dwindling populations while their aggressive neighbors bred huge potential armies. The *folie raisonnée* of the blustering nations that needed more

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ALKALINIZATION DURING SULFONAMIDE THERAPY

A NUMBER of investigators¹⁻⁵ have recommended the routine use of alkalis, in the form of sodium bicarbonate orally or sodium lactate parenterally, as an adjuvant to sulfonamide therapy. They have presented evidence to indicate that this tends to prevent crystalluria and its concomitant damage of the urinary tract. Daily doses of 15 to 24 gm. (average, 20 gm.) of sodium bicarbonate or 1500 to 2000 cc. of one-sixth molar sodium lactate solution (27 to 36 gr. of sodium lactate) are usually required to maintain the alkalinity of the urine for this purpose. It is claimed that clinical experience with these drugs has resulted in almost complete

elimination of urinary-tract complications (crystalluria, hematuria, renal colic and anuria).

It is known, however, that the administration of such large doses of a sodium salt may, in certain types of patients, result in the retention of water in amounts that may be serious and even dangerous. This may be expected particularly in patients with cardiac, renal or hepatic insufficiency of even mild degree and often occurs in pregnant women. Indeed Lyons and his associates⁶ have shown that water retention may result in normal persons from the ingestion of similar amounts of sodium bicarbonate. These investigators gave 50 gm. of sodium bicarbonate to each of six normal subjects over a period of forty-eight hours. They found an average increase of 400 cc. in the plasma volume and an average increase of 1.6 kg. in body weight, an increase of 14.4 per cent in the former and one of 2.3 per cent in the latter. Slightly greater increases were found after the ingestion of 40 gm. of sodium chloride over a similar forty-eight-hour period. Edema due to water retention is also frequently observed postoperatively in patients receiving parenteral injections of sodium chloride solutions containing equivalent amounts of sodium. Furthermore, the recommended amounts of alkaline drugs have a tendency to increase excretion of the sulfonamide drugs, thus necessitating the use of larger doses of these drugs to maintain the desired blood concentration.⁷ Should this increased excretion occur in a patient who also had water retention, the renal complications might be increased rather than eliminated, in spite of the greater solubility of the excreted drug in the alkaline urine.

Elsewhere in this issue of the *Journal*, Drs. Ohnysty and Wolfson present evidence that these difficulties may be overcome by substituting potassium salts, particularly potassium bicarbonate, for sodium salts in alkalizing patients during sulfonamide therapy. The use of potassium bicarbonate has the advantage of producing the same alkalinity in the urine and at the same time having a diuretic effect,⁸ instead of the water-retaining tendency of sodium salts.

The use of potassium salts instead of the sodium salts has been rejected by previous workers because of the possibility that abnormal cardiac

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THE PROBLEM OF POSTWAR SURGICAL TRAINING FOR RETURNING MEDICAL OFFICERS*

ALLEN O. WHIPPLE, M.D.†

NEW YORK CITY

THE subject of postwar training and rehabilitation of medical officers, now active in the Army, the Navy, the Marines and the Public Health Service in this country and on every continent and ocean, is closely linked with the plan and philosophy of the armed forces as they are functioning in this global war.

The experience of this country in the last war helping to win it but sharing an even greater responsibility in losing the peace was a sobering one. But the blind isolationists realized after the convincing evidences of the power and insane ambitions of Germany in Europe and the increasing encroachments of Japan in the Pacific that we were facing an inevitable conflict. But we were fortunate in having time to prepare for the war by getting our facilities mobilized during the early days of lend-lease, and the Nation was psychologically prepared for the draft and an all-out war effort before Pearl Harbor.

There was none of the flag-waving and impatient enthusiasm on the part of the citizenry and youth to enter this war that were evident in the last one. The young men and women faced the inevitable with a seriousness and a conviction that those of the World War I generation, not they, were responsible for the present situation in so deplorably losing the opportunities presented for winning the peace.

One of the outstanding differences between the conduct of the last war and the present one is the special training of the men in all branches of the service for their jobs. Because the armed forces were engaged in all parts of the world they have been given more careful selected training and more initiative than in the last war. The rapid development of fighting in the air, on the ground and on land under the ocean has produced weapons, machines and physical means of communication and

detection never conceived of in previous wars. This has resulted in the training and bringing out of initiative in literally millions of young people, male and female, that will demand expression, as soon as the war is over, in work and occupation that cannot be denied.

The last war, by and large, provided a type of experience in trench and stabilized warfare that was directly opposed to the later demands of civilian life. This war, because of its global distribution and its mobile character, is providing countless experiences that can be translated into success in civil life. Training programs and a more intelligent evaluation of previous experience, aptitudes and latent abilities have resulted in an incomparably more intelligent and efficient Army and Navy than we have ever had before, and a body of men and women who, because of this experience, will rightly demand a proper place in life on their return.

In a recent visit to our forces in Great Britain and North Africa I was impressed by the general concern of the soldiers and officers over four possibilities. First was the fear that war weariness and complacency at home would lead to a premature cessation of hostilities, — in which they were doing the fighting and dying, — which would again result in losing the peace. Second was a bitter resentment and anger over the conflict between capital and labor, resulting in strikes and interference with the war effort: the coal strike was threatening, and Lewis was more hated than Hitler. Third was apprehension regarding postwar opportunity and employment. Last was uncertainty regarding the utilization of their newly acquired experience and the means of further training to perfect themselves in these fields.

Just what will the answer be to this group of ten to thirteen million men and women as they return to civilian life? Do American businessmen, industrial leaders and professional groups believe that a World War I ideology and a Versailles Treaty attitude will be able to cope with this problem and provide leadership acceptable to these new veterans

*From the Department of Surgery, Columbia University.
Read at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

†Valentine Mott Professor of Surgery, Columbia University, director, Resbyterian Hospital.

babies to make bigger armies to fight for more territory for their expanding populations is typical of the type of inspired leadership with which we have no sympathy, although we must fear it. To enter into direct competition with it is serving no useful future purpose.

A declining population is no more undesirable than a rapidly increasing one—both lead eventually to race suicide, the one by stagnation or inundation and the other by mass starvation or total war, or both. A high fertility rate and large populations in themselves, moreover, are no guarantee against military exploitation by one's aggressive neighbors, as witness the plight of China and India.

The only reasonable answer is the more effective use of that intracranial organ by which man is supposed to be distinguished from the lower animals, for the control of population growths and selective breeding. When we use half the ingenuity in the breeding and feeding of man that we now direct toward the science of animal husbandry, we may find that brave new world in sight.

MASSACHUSETTS MEDICAL SOCIETY



Medical societies in Kansas, Missouri and New Hampshire recently approved the establishment of nonprofit plans for the voluntary prepayment of medical and surgical bills resulting from hospitalized illnesses, injury and maternity care. This brings to eleven the number of states in which medical prepayment plans are co-ordinated with Blue Cross hospital-service plans. States in which medical plans were previously established and co-ordinated with Blue Cross plans are California, Colorado, Michigan, North Carolina, Delaware, Pennsylvania, Massachusetts and New York.

Of the above plans, by far the largest is Michigan Medical Service, sponsored by the Michigan State Medical Society. From recent reports one person in nine in Michigan is covered by this medical-care insurance, and during the four years of its life, Michigan Medical Service has paid to physicians in the state more than \$6,000,000.

The Michigan plan is beginning to prove that the profession itself can solve the health problems facing the nation and that physicians operating under the present free system have something

tangible to offer as a substitute for governmental medicine. Here in Massachusetts we have the same opportunity to solve the problem of a better distribution of medical care among the lower income groups and to forestall compulsory health programs but only if all the physicians in the Commonwealth give their enthusiastic and united support to the Blue Shield plan.

Doctors who have not yet become participating physicians are urged to communicate with the Blue Shield regarding participation in the plan. Doctors who have already become Blue Shield participating physicians are urgently requested to spread the gospel of Blue Shield protection among their patients and to distribute literature regarding the plan in their waiting rooms.

It seems unnecessary to add that the physicians who participate in the Blue Shield will be better off financially than they would be out of the plan. Figures are not available to show how much of the \$6,000,000 of disbursements by the Michigan Medical Service would have been collected by the doctors themselves, but if it is true that only 80 per cent collections are made by the profession, then the Michigan physicians would have received only \$4,800,000 for the amount of services.

The time to make an impressive record of achievement is now. When the war ends, and thousands of medical officers return to civilian ranks after witnessing the impressive and efficient distribution of governmental medicine to the 12,000,000 Americans in the armed forces, it may be too late. Furthermore, the 12,000,000 recipients of this same kind of medical care will undoubtedly have a good deal to say in the matter, but only if the Blue Shield has failed in its attempt to solve the problem.

In a recent survey in California, several interesting facts were established. Some of them are as follows: 88 per cent of the people think that the majority of doctors are doing a good job for the people; 34 per cent are against federal medicine; 50 per cent are in favor of federal medicine, and 16 per cent have not made up their minds. The question is, Why is there such a demand for federal medicine when there is such a high approval of the profession? The answer is, People believe that the cost of scientific medicine is too high. The conclusion is obvious. When something is needed by all the people but is too costly for them, eventually it is socialized so that it becomes available to all.

DEATH

JONES — Lombard C. Jones, M.D., of Falmouth, died August 17. He was in his seventy-ninth year.

Dr. Jones received his degree from Harvard Medical School in 1892. He was a member of the American Medical Association and the Harvard board of overseers.

His widow, a son, two step-daughters, two sisters and a brother survive.

(Notices on page xix)

to obtain surgical training in our well-equipped and adequately staffed hospitals after the war will be far greater than ever before. This will only complicate our own difficulties in providing proper facilities for medical officers seeking further surgical experience.

Out of all this complicated and difficult problem there may develop a clearer and more definite realization on the part of the medical profession and the laity that surgery, as a branch of therapy in the science of medicine, should be limited to those having adequate resident training, responsibility and experience. There is an increasing recognition of the importance of such training, as shown by the insistence of hospital boards that appointments to their surgical staffs be made from surgeons adequately trained and qualified by the boards of the several specialties.

The mortality and morbidity rates of the patients of properly qualified surgeons as compared with those of the casual operator engaged in general practice are so obvious to intelligent boards of management that they are insisting on limiting the surgery in their hospitals to qualified surgeons. The high standards of wound healing, preoperative and post-operative care and follow-up results that one finds in a well-trained surgical resident on a three-to-five-year program in teaching hospitals are so far superior to the oldtime self-made amphitheater and circus-performing surgeon that there is no comparison between them. One of the tragedies of this war is the interruption of the well-established program of resident training in so many of the hospitals of this country. It should be our aim and determination to restore this program as soon as the exigencies of war permit.

522 West 168th Street

EPIDEMIC TYPHUS FEVER AND OTHER RICKETTSIAL DISEASES OF MILITARY IMPORTANCE*

C. S. STEPHENSON, M.D., D.S.C. (hon.)†

WASHINGTON, D. C.

THE rickettsial diseases of military importance are epidemic typhus fever, tsutsugamushi fever, trench fever, murine typhus fever and Rocky Mountain spotted fever. Although only a few cases of murine typhus fever have occurred in the military personnel during this war, some of them have occurred under circumstances that raised epidemiologic questions that had to be answered. The Rocky Mountain spotted fever group is at this time of least importance, since there is no large body of troops stationed in the endemic area.

Trench fever has been classified as a rickettsial disease and is louse borne. Organisms of the rickettsial group have been reported as recovered from lice and their feces fed on patients ill of trench fever. These organisms have subsequently infected volunteers. Trench fever disappeared following World War I before it was possible adequately to study the disease. It is again reported in Europe, however, and if future military operations require prolonged trench warfare it may recur there. Owing to the efficiency of the newer methods of louse control it should not produce the damage it caused in the last war.

With the exception of Q fever and trench fever, this group of diseases produces in the serums of patients agglutinins for the X strain of the proteus

bacillus — *Proteus vulgaris*. There is no known strain of proteus bacillus that agglutinates with Q-fever serums, and nothing has been reported concerning agglutinins in trench fever. The Weil-Felix reaction — agglutination of the proteus-bacillus group — is used to differentiate typhus fever, Rocky Mountain spotted fever, tsutsugamushi fever and other febrile exanthematous diseases. The serums of patients suffering from spotted fever and typhus fever agglutinate with OX19 and OX2 strains, whereas the serums of patients with tsutsugamushi fever agglutinate the OXK strain.

EPIDEMIC TYPHUS FEVER

The synonyms of epidemic typhus fever are as follows: shipboard fever, jail fever, putrid fever, petechial fever, typhus exanthematicus, *Fleckfieber* (German), *typhus exanthématique* (French), *el tabardillo* (Spanish) and *typho-esantematico* (Italian). It may be defined as an acute infectious disease caused by *Rickettsia prowazki*. In the majority of cases the onset is abrupt and is accompanied by a fever lasting about fourteen days, usually followed by a critical fall or in some cases by a rapid lysis of temperature. A striking feature of this disease is a "rose-spot" eruption that appears from the fifth to the sixth day of the disease, usually on the abdomen or loins and extending over the trunk and extremities. Under pressure the rash fades, radiating in a stellate form from the middle of the rose-red macule or papule. Other prominent features of the disease are profound stupor

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

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†Formerly, rear admiral (MC), U.S.N., and director, United States of America Typhus Commission.

of World War II? If so, we may be sure of a fusion of these millions of men and women and their families, resentful of such an attitude and ready to follow radical leadership into the most powerful pressure group this country has ever known, with a block of votes that will make any Congress dance to any tune.

What has been said about the men in the service in general applies equally to the medical officers in the armed forces. But they have additional problems peculiar to their profession. The older group have left practices of various kinds of work and compensation. Regardless of the efforts of their associates in their communities, not in military service, to preserve the work of these men, they realize that on their return to their homes they will have to salvage the greater part of their lost practices. The younger group, called to service before completing their residencies and with only short-term internships, have a common query: How and where can I complete my training? Many of these men, as well as those of the older group, have had to do varying amounts and kinds of war surgery, realize their lack of training and are anxious to get a more adequate experience in civilian surgery. A recent analysis of a pilot questionnaire sent to surgical officers in the Army shows that 77 per cent of the men graduating from medical schools between the years 1936 and 1942 desire further training as surgical residents.

A recent address by Surgeon General Kirk paid unstinted praise to the surgeons in the war zones and in military hospitals in reducing the mortality in casualties to a record 3.5 per cent, and stated that this was due to the selection of surgeons with adequate resident training and from those qualified by the several qualifying boards. Unfortunately, the accelerated medical curriculum and the limitation of postgraduate training to a nine-month internship and a limited number of men in the 9-9-9 plan — a program followed at the insistence of the Army and Navy for military reasons — have effectively stopped the supply and the training of the very group of surgeons who have been responsible for the high standard of service and accomplishment referred to by the Surgeon General. This is indeed a serious situation if the war continues for more than a year, for poorly educated and inadequately trained surgeons will be sent to do the most difficult kind of traumatic surgery. The goose laying the golden eggs is being killed.

This question of how to provide postwar training in surgery for men returning from military service is being discussed by many national medical and surgical organizations. Questionnaires are being sent to all the medical officers here and abroad by the American Medical Association and the American College of Surgeons. There is danger of too many cooks' spoiling this particular broth. The subject is being discussed in Washington,

in and out of Congress, but beyond providing for financial aid to the returning medical officer for periods equal to his time in the service, no concrete ideas have thus far appeared in Washington.

It is obvious that the many veterans' hospitals, already built and planned, to provide several hundred thousand beds for returning casualties, must be staffed. How to obtain qualified surgeons for these hospitals is one of the postwar problems that is not a congenial or promising topic in Washington. The Clark bill in Congress, not yet reported out of committee, provides, among other things, that the postwar training of medical officers shall be under the Veterans Bureau. The purpose of this bill is obvious. But how adequate will these veterans' hospitals be for such training? This will depend on their location, their proximity to medical teaching institutions and their relations with them and on the ability and experience and compensation of the surgeons and physicians appointed to the staffs of these hospitals. Unless the selection and appointment of the staffs of these hospitals are of an entirely different character from those of the last war, the postwar training of returning medical officers in veterans' hospitals will be a tragedy.

In the questionnaire referred to only 11 per cent of those replying indicated a desire to remain in governmental service, and a smaller percentage desired to work in veterans' hospitals.

In decelerating the medical-school curricula on the basis of the original four-year plan, which is being proposed beginning in 1945, there will be in the following three years a period of nine months to one year when there are no medical students available for internships. This may be of great help in providing places for medical officers, demobilized on a staggered program, to get further hospital training. But it will require the intelligent, patriotic and far-seeing co-operation of the medical boards and boards of managers of the better hospitals all over this country to rearrange the intern and resident training program to provide positions and opportunities for such training. The normal standards of surgical service have been badly compromised, and the ability of hospitals seemingly to function under war conditions with limited and poorly trained assistants will require a re-education of boards of managers to provide room and opportunity for these medical officers returning and desiring further training.

Undoubtedly most of the hospitals will give first choice and priority to the men who as interns or first-year and second-year residents left these hospitals for military service. But in addition a limited provision should be made in all these hospitals for men of demonstrated ability as medical officers to get further resident experience.

It must be realized that with the complete disorganization of medical centers and hospitals in Europe, the pressure from that and other continents

obtain surgical training in our well-equipped and adequately staffed hospitals after the war will be greater than ever before. This will only complicate our own difficulties in providing proper facilities for medical officers seeking further surgical experience.

Out of all this complicated and difficult problem there may develop a clearer and more definite specialization on the part of the medical profession and the laity that surgery, as a branch of therapy in the science of medicine, should be limited to those having adequate resident training, responsibility and experience. There is an increasing recognition of the importance of such training, as shown by the insistence of hospital boards that appointments to their surgical staffs be made from surgeons adequately trained and qualified by the boards of the several specialties.

The mortality and morbidity rates of the patients of properly qualified surgeons as compared with those of the casual operator engaged in general practice are so obvious to intelligent boards of management that they are insisting on limiting the surgery in their hospitals to qualified surgeons. The high standards of wound healing, preoperative and postoperative care and follow-up results that one finds in a well-trained surgical resident on a three-to-five-year program in teaching hospitals are so far superior to the oldtime self-made amputee and circus-performing surgeon that there is no comparison between them. One of the tragedies of this war is the interruption of the well-established program of resident training in so many of the hospitals of this country. It should be our aim and determination to restore this program as soon as the exigencies of war permit.

522 West 168th Street

EPIDEMIC TYPHUS FEVER AND OTHER RICKETTSIAL DISEASES OF MILITARY IMPORTANCE*

C. S. STEPHENSON, M.D., D.S.C. (hon.)†

WASHINGTON, D. C.

THE rickettsial diseases of military importance are epidemic typhus fever, tsutsugamushi fever, trench fever, murine typhus fever and Rocky Mountain spotted fever. Although only a few cases of murine typhus fever have occurred in the military personnel during this war, some of them have occurred under circumstances that raised epidemiologic questions that had to be answered. The Rocky Mountain spotted fever group is at this time of least importance, since there is no large body of troops stationed in the endemic area.

Trench fever has been classified as a rickettsial disease and is louse borne. Organisms of the rickettsial group have been reported as recovered from lice and their feces fed on patients ill of trench fever. These organisms have subsequently infected volunteers. Trench fever disappeared following World War I before it was possible adequately to study the disease. It is again reported in Europe, however, and if future military operations require prolonged trench warfare it may recur there. Owing to the efficiency of the newer methods of louse control it should not produce the damage it caused in the last war.

With the exception of Q fever and trench fever, this group of diseases produces in the serums of patients agglutinins for the X strain of the proteus

bacillus — *Proteus vulgaris*. There is no known strain of proteus bacillus that agglutinates with Q-fever serums, and nothing has been reported concerning agglutinins in trench fever. The Weil-Felix reaction — agglutination of the proteus-bacillus group — is used to differentiate typhus fever, Rocky Mountain spotted fever, tsutsugamushi fever and other febrile exanthematous diseases. The serums of patients suffering from spotted fever and typhus fever agglutinate with OX19 and OX2 strains, whereas the serums of patients with tsutsugamushi fever agglutinate the OXK strain.

EPIDEMIC TYPHUS FEVER

The synonyms of epidemic typhus fever are as follows: shipboard fever, jail fever, putrid fever, petechial fever, typhus exanthematicus, *Fleckfieber* (German), *typhus exanthématique* (French), *el tabardillo* (Spanish) and *typho-esantematico* (Italian). It may be defined as an acute infectious disease caused by *Rickettsia prowazeki*. In the majority of cases the onset is abrupt and is accompanied by a fever lasting about fourteen days, usually followed by a critical fall or in some cases by a rapid lysis of temperature. A striking feature of this disease is a "rose-spot" eruption that appears from the fifth to the sixth day of the disease, usually on the abdomen or loins and extending over the trunk and extremities. Under pressure the rash fades, radiating in a stellate form from the middle of the rose-red macule or papule. Other prominent features of the disease are profound stupor

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†Formerly, rear admiral (MC), U.S.N., and director, United States of America Typhus Commission.

and deafness, which may continue for months after the patient is well.

Epidemic typhus fever has probably killed more persons during periods of wars and famine than has any other disease. Medical history is indebted to Fracastorius for describing the first epidemic of typhus fever that can be readily recognized as such, as well as subsequent epidemics occurring in Italy from 1505 to 1530. Hirsch wrote of typhus fever as follows:

The history of typhus is written in those dark pages of the world's story which tell of the grievous visitations of mankind by war, famine and misery of every kind. In every age, as far back as the historical inquirer can follow the disease at all, typhus is met with in association with the saddest misfortunes of the populace; and it is, therefore, a well-grounded surmise that the numerous pestilences of war and famine in ancient times and in the Middle Ages, which are known to us . . . had included typhus fever as a prominent figure among them.

The scientific epidemiology of typhus fever began in the early part of the sixteenth century. It was rife over the greater part of Italy from 1505 to 1530. Soon thereafter numerous epidemics were reported from almost all the European states. The political and social disturbances of the seventeenth and eighteenth centuries and the first thirty years of the nineteenth served to spread repeated epidemics to all parts of Europe.

The epidemiologic records of the eighteenth century reveal that there was scarcely a year in that period in which great or small typhus-fever epidemics did not occur. In brief there are four periods of special importance. The first period began about 1690 and ended about 1720. Austria, Germany and Hungary were particularly involved, and Ireland had three severe epidemics, the two last having spread to England and Scotland. The years 1734-1744 comprise the second period, when Central and Eastern Europe were involved. It was a war pestilence in company with typhoid fever and the dysenteries. It is noteworthy that of all the great wars of which there is record, the American Civil War and the Franco-Prussian War in 1870 are the only ones in which epidemic typhus fever did not have a prominent place. The Seven Years' War and the war between England and Spain ushered in the third period (1757-1775). A severe famine occurred in Europe at that time and produced conditions favorable for the disease to spread. The revolutionary wars in France started the fourth period, which was by far the severest epidemic period of typhus fever in the eighteenth century. This period began about 1790 and lasted until the conclusion of peace in 1815. During that time typhus fever spread all over Europe. It was severest in the war-ravaged countries, but did not spare populations remotely removed from military concentrations or the travel routes of troops.

The Western Hemisphere had its first experience with epidemic typhus fever in Mexico, following the Spanish Conquest, where it became epidemic

in 1530. Pizarro began the conquest of Peru in 1526, and typhus fever soon appeared in the high lands of South and Central America, where it remains as an endemic disease known as *tobardillo*. Canada's first experience with the disease appears to have been in 1659, with several recurrences in the eighteenth and nineteenth centuries. The first great wave of Irish immigration to Canada was in 1847, the immigration and quarantine records showing that 84,445 persons immigrated to Canada that year. Of this number 75,540 came from Ireland. Among these, 30,265 persons contracted typhus fever. Of this number, 5293 died during the various voyages at sea, 8012 at Quebec and 7000 at Montreal—a total of 20,305 deaths. Several times during the eighteenth and nineteenth centuries typhus fever appeared in the seaports of the United States. Philadelphia had its last reported epidemic in 1883 and New York in 1893. Flippin in 1931 reported that 27 cases of epidemic typhus fever had occurred in Philadelphia since 1911. For some unaccountable reason louse-borne typhus fever has never established an endemic focus in either Canada or the United States.

The important endemic foci of typhus fever at the present time are China, Russia, Turkey, Syria, Iran, Irak, Arabia, Afghanistan, Spain, parts of France, eastern Europe, Germany, Italy, North Africa, parts of Central Africa and the mountainous sections of Central and South America.

Early in the present war, typhus fever began to increase in certain parts of Europe, North Africa and the Middle East. In 1942 the reported increase became so important that several conferences between representatives of the Army, Navy and United States Public Health Service were called and in the fall of that year the United States of America Typhus Commission was established by executive order of the President.

The most important epidemiologic features of epidemic typhus fever are as follows: It spreads rapidly among distressed populations disorganized by famine or war. It usually appears first in concentration camps, prisons and slums. It is a disease of cold weather; Hirsch analyzed one hundred and forty-seven epidemics and reported that thirty reached their peak in spring, twenty-eight in winter and spring, eighteen in autumn, seventeen in summer and fourteen in autumn and winter. It is associated with a louse-ridden population, and is readily transmitted from person to person by the body louse. An attack usually confers a long immunity; some investigators believe that the severer is the attack the longer is the immunity.

Epidemic typhus fever is transmitted by the louse *Pediculus humanus*. Nicolle, Conte and Conseil in 1909 proved by experiment that the chimpanzee could be infected with the disease by the injection of a small amount of blood from a human case in the active stage of the disease. They then infected

onkeys and proved that it could be transmitted from monkey to monkey by bites of the infected body use (*Ped. humanus* var. *corporis*). This work was confirmed in the United States in 1910 by Ricketts and Wilder. From the work of Goldberger and Anderson it seems clear that the head louse (*Ped. humanus* var. *capitis*) may transmit the disease under experimental conditions. It is not, however, regarded as an important vector.

Hume reports that the physicians in Serbia in the last war recognized the louse as the vector but believed that there were other methods of infection, especially favoring the inhalation theory. It was shown in 1923 by Arkwright and Bacot that rickettsias could survive in the feces of infected lice at room temperature for eleven days. The high mortality rate among physicians, nurses and orderlies in typhus-fever epidemics — especially since this group of persons is nearly always surrounded by many precautions against lice — strongly suggests that actual contact with lice is not always necessary. Since rickettsias are known to remain viable and to retain their virulence for at least eleven days in dried feces of lice, since experimental animals have been infected by intranasal inoculation, and since laboratory workers and others have contracted typhus fever in an unexplained manner, it seems highly probable that the inhalation of rickettsias in dried feces of lice has been responsible in some cases.

The most frequently reported period of incubation is eight to twelve days, but the period varies from five to fifteen days. The onset may be accompanied by a chill, usually not severe, which may be preceded by a few days of malaise, nausea, severe headache and loss of appetite. The fever usually reaches its maximum by the end of the first week. Morning remissions of fever are frequently seen, but are usually not very marked in the second week, by the end of which time the temperature usually falls by a rapid lysis, except that in complicated cases the patient does not become afebrile until the sixteenth day.

One of the most difficult symptoms to control is severe headache. Cardiac weakness and profound prostration may be seen from the very onset of the illness, and are usually most prominent in the second week. Constipation is a frequent and troublesome feature. The teeth are covered with sordes, which requires strict nursing care to control. Otitis media and parotitis are connected with this condition. The conjunctivas are injected. All the symptoms, especially the cardiac ones, may become exaggerated on the appearance of the rash. Nose-bleed may occur.

Mental disturbance is usually seen by the end of the first week and may vary from confusion, disorientation and restlessness to terrifying hallucinations that sometimes end in the patient's jumping from a window. Some of these symptoms

may remain in varying degrees of severity for weeks or months after the acute illness is over. Owing to the circulatory disturbance, gangrene, especially of the toes and less frequently of the fingers, is sometimes seen. It is often bilateral.

In uncomplicated cases with recovery there is a dramatic change in the condition at about the fourteenth day. The temperature falls and the mental condition greatly improves. In older patients the prostration and cardiac weakness may remain for a considerable period of time. As a rule younger patients make a more rapid recovery. Sequelae are rarely seen.

Cough is extremely frequent and may appear from the beginning of the illness, but is usually most annoying on the appearance of the rash. By the beginning of the second week the cough usually becomes less troublesome and various rales may be heard. Death from bronchopneumonia is frequent. Physicians in the Middle East report an unusual number of cases of bronchopneumonia in the present epidemic. Several physicians with extensive experience in this epidemic believe that some degree of bronchopneumonia is always present. They point out that in previous epidemics there was such a shortage of physicians that careful physical examinations were frequently impossible.

The eruption appears usually around the fourth day about the flanks and axillas and spreads to the chest and back. It is usually more pronounced on the back. It is seldom seen on the face, but is seen in the palms and on the soles. The rash lasts a varying time — from a few days to weeks. Occasionally markedly hemorrhagic rashes are accompanied by hematuria, hematemesis and melena which indicate a poor prognosis. The rash at onset easily disappears on pressure, leaving stellate radiations. Later it does not disappear so easily on pressure and becomes petechial.

A prominent feature is cardiac weakness due to myocardial damage. The heart sounds are weak, with a rapid, irregular pulse. The blood pressure is often quite low. Bradycardia is frequently seen in convalescence.

There is no characteristic blood finding. Leukopenia may be present in the first few days, but in uncomplicated cases the white-cell count rises to 10,000 or 15,000.

Albuminuria may be present from the onset, but disappears with convalescence.

Diagnosis

The most important laboratory finding is a positive Weil-Felix reaction during the second week of the disease. It reaches its height during convalescence and may rapidly disappear. For diagnostic purposes a test should be made in all suspected cases and repeated late in the second week. With a good antigen the serums of patients ill of typhus fever frequently reach titers of 1:10,000 to

1:100,000. The OX19 strain of the proteus bacillus is most frequently used, because it is more frequently agglutinated than is OX2. This reaction has no practical value in differentiating Rocky Mountain spotted fever from typhus fever. There are diseases not caused by the rickettsias that may show a titer in dilutions of 1:320 and occasionally higher.

An important recent advance is the utilization of the complement-fixation test in the diagnosis of typhus. In this test rickettsias of epidemic typhus fever are used as an antigen. The test becomes positive in the second week and may remain positive for the life of the patient.

On gross examination little is seen at autopsy except the fading rash, the complicating bronchopneumonia and splenic enlargement. Fraenkel in 1914 described the essential lesion as distinguished by injury to the capillary and precapillary vessels, characterized by proliferative changes in the endothelium of the arterioles and arterial capillaries, followed by necrotic changes, chiefly in the vessels of the skin, myocardium and central nervous system. There is a perivascular infiltration of small round cells. The lesions, which are microscopic in size, are most frequent in the skin, heart, great vessels, adrenal glands, testes, kidneys and brain, with the cerebral cortex usually the most involved part. Quite characteristic are the small paracapillary nodes of microglia. Plasma-cell infiltration and frequent thrombi have been reported. Splenic hemorrhages are frequently seen.

No specific treatment has proved of value. Many of the more recent chemotherapeutic agents have been used, with little success; in several cases there was evidence of harm from them. Convalescent human serums and serums from horses inoculated with rickettsias have been tried, with little benefit. A hyperimmune rabbit serum has been used in a small series of cases, with indications that it is valuable.

For the relief of the headache, acetylsalicylic acid is frequently not enough and resort to codeine or morphine is necessary. Constipation should be controlled, preferably with mild laxatives or enemas. Digitalis is of value in cases showing cardiac failure. Cardiac depressants are to be avoided. Every precaution should be taken to conserve the patient's strength. Good nursing is essential to prevent bedsores. In severe cases, particularly in elderly persons, the patient should be confined to bed until convalescence is well advanced.

This disease can be controlled by the destruction of lice. In a campaign against epidemic typhus fever, measures should be taken to include all persons in infected districts. This can only be done by house-to-house inspection, with removal of patients to hospitals and disinfection of all contacts, their clothing and houses. A quarantine should be established and all persons coming from

typhus-infected areas should be treated as contacts. Clothing and bedding can be disinfested either by heat or by chemical means, that is, by the use of louse powders. A recent popular article reports that 1,300,000 persons were deloused in Naples in January of this year and that one application of the powder to the clothing was effective for about six weeks.

The body louse nests in the seams of clothing and the louse-infested person should be bathed and the hair of the body and head should be clipped. In female patients great resistance to clipping is frequently encountered. Where this resistance is based on social customs or religious beliefs, it is far better to resort to oil and chemicals to kill the lice than to come in conflict with folkways. The new powders effectively solve the problem.

Physicians, nurses and orderlies in hospitals caring for typhus-fever patients should be provided with closely woven white-cotton, louse-proof garments fashioned like coveralls and open at the neck, wrists and ankles. Socks should be pulled over the bottoms and rubber gloves used on the wrists, and the neckband should be tightly closed. Because of the probability that infection has occurred from the inhalation of dried feces of lice, great care should be exercised in examining patients and in handling their bedding and clothing.

Several types of vaccine have been prepared for immunizing against typhus fever. Attenuated living rickettsias by heat or other means have been employed, but the inherent danger of using vaccines of these rickettsias has been shown by the fact that typhus fever has been produced by some of them. Rickettsias killed by phenol or formaldehyde are also used. The Weigl vaccine is reported to give good immunity, but it cannot be produced in large quantities. It is made by the injection of a suspension of rickettsias into the rectums of lice, which are subsequently fed to typhus fever-immune persons, after which the lower intestines are removed and prepared as a suspension that is used as a vaccine. About 200 lice are required to prepare a vaccine for one person. Vaccines made from killed rickettsias from the lungs of intranasally infected rats, mice or rabbits have been used.

The vaccine in use by the United States armed forces is the modified Cox vaccine, which is made from killed rickettsias from the developing yolk sac of the chick embryo. This vaccine gives good results in laboratory animals, but lacks adequate field tests in human beings. Typhus fever has occurred in a number of laboratory workers and in about 50 members of the armed forces, all of whom have been vaccinated, but there have been no deaths. It is the consensus that this vaccine has greatly modified the course of the disease in those who have acquired typhus fever subsequent to vaccination. It is used in a series of three inoculations.

ons, with a booster dose every few months when typhus-fever area.

ENDEMIC TYPHUS FEVER

The synonyms of endemic typhus fever are: rine typhus fever, Brill's disease and Mexican hus fever (*Tabardillo*). The causative agent been named *R. mooseri*. Brill in 1898 described orm of febrile disease of unknown origin that embled typhoid fever but gave a negative Widal ction. He noted that epidemiology of the disease ured from epidemic typhus fever in that it urred sporadically in a louse-free population and ; milder in character than the latter and had a erent seasonal occurrence. These facts caused him suspect some other vector than the louse as possible.

Maxey's work in the southern United States closed that most of the cases occurred among d handlers. This caused him to conclude that e reservoir in nature is the common rat. It seems ely that other rodents are also responsible.

Zinsser studied the records of 538 cases of Brill's eadise that occurred in Boston and New York ty between 1910 and 1933. Of these, about per cent occurred in foreign-born persons who d migrated from Russia. Ninety-seven per cent all the cases from 1910 to 1920 were in Jews, d over 80 per cent of the patients came from ussia. Zinsser believed that the cases of Brill's eadise represented recrudescences of infections quired in Europe.

Endemic typhus fever has occurred in all the utheastern states and as far north on the East ast as Boston, in the coastal cities on the West ast and in Texas. In 1929 the human cases ere largely limited to towns and cities. Nashville, ennessee, had about 75 cases in 1941. There e additional foci in Cincinnati and Cleveland, io.

Since endemic typhus fever became well known the United States it has been found in many parts the world, especially in coastal cities. It is known o exist in Australia, the Philippines, China, Indo-hina, Manchukuo, Malaya, Syria, Lebanon, Pal-stine, Egypt, Greece and southern Europe. In frica it was believed that many cases of endemic yphus fever were diagnosed as epidemic; however, ll the strains isolated by the United States of merica Typhus Commission are of the endemic ype.

The epidemiologic aspects of the disease are as ollows. The peak of prevalence is in the late sum-ner and fall. In the United States the disease as occurred most frequently among workers in ood-handling establishments. The literature re-ords that human cases are associated with rat arborages. (I saw 6 cases in Australia in September,

1943, in which connection with rats, mice or fleas seemed highly improbable.) The disease is not con-fined to slums. Transmission from person to person by contact with rat fleas has not been proved.

Except for the milder course of the disease the clinical features are identical with those of epi-demic typhus fever. The rash does not usually appear before the fifth day, and except in severe cases is not so extensive as in epidemic typhus fever. In mild cases only a few macules appear, and they may disappear in a few days. The general symptoms are milder.

The mortality rate in the United States is below 5 per cent, and most of the deaths occur in persons over forty-five years of age. In the Middle East, physicians believe that a careful compilation of statistics would reveal a higher fatality rate. This may be explained by the present food conditions. The general food supply is well below that of normal times, whereas in the United States the experience with murine typhus fever has been confined to a population not under stress of war and not living on such restricted subsistence levels.

This disease has frequently been confused with drug rashes, typhoid fever and meningococcemia. A diagnosis cannot be made until the rash appears. In localities where epidemic typhus fever, Rocky Mountain spotted fever and tsutsugamushi disease occur the diagnosis must be established by labo-ratory methods. The Weil-Felix reaction is positive in high titers.

In the light of the present knowledge the control of endemic typhus fever rests on the control of the rat population. The case against the rat is sufficiently strong, because of other diseases and economic considerations, to cause the medical pro-fession to increase the fight against it. It has been estimated that the rat population in the United States is in excess of 250,000,000. In the opinion of competent mammalogists this estimate is too low. They believe that each rat consumes \$2 worth of food and damages \$20 worth of food a year. This economic waste runs into billions of dollars and is entirely unjustified in peacetime; in war-time with world-wide food rationing it is intolerable. Bubonic plague has recurred in Palestine, and if it should be introduced into one of our eastern seaports it would be necessary to destroy rats on board ships sailing from a foul to a clean port. This would seriously interfere with wartime ship-ping.

It is extremely interesting to note that medical men have been slow to employ trained mammal-ologists in the fight against rats, yet they have extensively employed entomologists in the control of disease-bearing mosquitoes.

Vaccines have been prepared from the rickettsias of endemic typhus by the same technics as for epidemic typhus fever. They show good protection

in laboratory animals, but there is no adequate experience with them in human populations.

TSUTSUGAMUSHI FEVER

The synonyms for tsutsugamushi disease are kedani mite disease, Japanese river fever and mite (scrub) typhus fever. Until the advent of World War II the American literature has been singularly lacking in reference to this disease.

Japanese physicians claim that the disease has been recorded for more than a thousand years. The first clinical report was published by Palm in 1878. Hayashi first named the organism causing this disease in Japan, *R. tsutsugamushi*. Kawamura and Imagawa worked with the organism and identified it as *R. akamushi*. This work was confirmed by Ogata who retained the original name *R. tsutsugamushi*. There is excellent reason to believe that these organisms are identical. Lewthwaite and Savor did exhaustive cross-immunity tests and showed the similarity between scrub typhus fever and tsutsugamushi disease by both intraocular and intradermal reactions in rabbits and monkeys. From cross-protection tests between the rickettsias of Samatran fever and the tsutsugamushi disease of British Malaya performed on monkeys and rabbits it appears that these diseases are identical. In addition to these reasons, it should be borne in mind that travel in those parts of the world is sufficiently great so that persons could easily be transported to those areas well within the period of communicability of this disease and infect the vector and animal reservoir.

In Japan the larval form of the harvest mite locally known as the kedani mite (*Trombicula akamushi*) is the vector of this disease. There are several species and variants within species of trombicula, and they may be vectors in different localities. Little is known of the habits of the trombicula. The larvae are microscopic six-legged creatures that move along the ground or cling to the vegetation until they attach themselves to a passing man, bird or animal. The eggs are laid 8 to 10 cm. under the surface of the ground and when hatched pass through several stages to the adult form. Animal and bird life is abundant in Australia and the islands of the Southwest Pacific and provides the necessary blood meal for these larval mites. The evidence is that the larval mite is infected from the parent and passes the rickettsia on to man. Much work is needed before a final answer can be given on the relation between the several variants of trombicula. At least three species are under suspicion by the Australian and United States Army medical officers. The trombicula larvae attack man on all parts of the body, but the most frequent sites are the scrotum, groin and armpits. Numerous ticks are found in Australia and the islands of the Pacific and until proved innocent should be regarded as additional vectors.

Rats are abundant in the islands of the Pacific, and it appears likely that the local rat is the principal reservoir. Gunther, however, has listed some seventeen hosts for the larval mite. These include such birds as the bush fowl, swamp hen and parrot. It seems probable that migratory wild fowl are likewise hosts and spread the mites from one island to another. Lizards are frequent in these islands and also have been known to be infested with mites.

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sitive about the end of the second week. A few
ses never became positive. Convalescence was
olonged.

The American literature contains no reports of
distinctive gross lesions. Lewthwaite in his study
rural tropical typhus fever in the Malay Penin-
ula found petechial hemorrhages in the heart,
ngs, alimentary tract and kidneys. The brain
owed perivascular infiltrations more especially
equent in the pons and medulla and also occurring
the cerebellum. Thrombus formation was noted
some of the capillaries.

In the endemic area the diagnosis should not be
difficult, since the history and initial lesion are
uite helpful. The presence of OXK and the ab-
ence of OX2 and OX19 agglutinins should clear
he diagnosis.

It is generally agreed that the most important
ector in the treatment of tsutsugamushi disease
absolute bed rest and symptomatic treatment.
here is a difference of opinion about the adequacy
f acetylsalicylic acid in the control of headache.
hlum and Lipshutz discontinued the use of codeine
ecause of abdominal distention, which interfered
ith fluid intake. Several Australian medical
fficers found acetylsalicylic acid inadequate. Gen-
rally the patients with pneumonic signs were given
ne of the sulfonamide drugs in adequate doses, with
o appreciable results. All agree that there is a
itamin deficiency. The use of digitalis was dis-
appointing, as was the use of oxygen. The use of
edatives in adequate doses cannot be overrated.

Convalescent serum was considered, but was
ot used because there is no exact knowledge when
he blood is free of rickettsias and because of pos-
sible shock following its use.

The wearing of mite-proof clothing has been
recommended by the Japanese and others, but
anyone who has attempted to work in the endemic
areas of the tropics will realize that this measure
s impractical. Excellent results from the use of
insect repellents have been reported by the Aus-
tralian medical authorities. Camp sites should be
carefully selected and if possible be prepared by
natives. The grass should be cut to destroy the
habitat of possible vertebrate reservoirs and mites.
Rigid control of rats is necessary. Men should be

provided with hammocks and should not sleep on
the ground. Spraying the ground with a petroleum
emulsion of one of the new insecticides should be
considered. The value of any repellent is in its
proper use. Those exposed in an endemic area
should be carefully instructed in the use of repel-
lents and especially told to dust their socks and
trousers carefully. If the clothing is thoroughly
treated with insecticide there is no reason to expect
a mite to pass through its meshes.

TRENCH FEVER

During World War I trench fever was known as
five-day or Wolhynia fever. This disease dis-
appeared after the war and its true relation with the
rest of the rickettsial diseases is unknown. It is
louse borne and extracellular rickettsias have been
found in lice fed on patients ill with this disease.
Rickettsias are found in the feces of lice fed as
indicated. There is no report of agglutination of
X strains of proteus bacillus by patients' serums.
The incubation period is from five to twenty days.
The onset is sudden, with a quick rise of temper-
ature, which may last from a few days to over a
week. A number of relapses is the rule, which makes
this an important contributor to lost days. There
is no specific treatment. Prevention is by control
of lice.

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in laboratory animals, but there is no adequate experience with them in human populations.

TSUTSUGAMUSHI FEVER

The synonyms for tsutsugamushi disease are kedani mite disease, Japanese river fever and mite (scrub) typhus fever. Until the advent of World War II the American literature has been singularly lacking in reference to this disease.

Japanese physicians claim that the disease has been recorded for more than a thousand years. The first clinical report was published by Palm in 1878. Hayashi first named the organism causing this disease in Japan, *R. tsutsugamushi*. Kawamura and Imagawa worked with the organism and identified it as *R. akamushi*. This work was confirmed by Ogata who retained the original name *R. tsutsugamushi*. There is excellent reason to believe that these organisms are identical. Lewthwaite and Savoor did exhaustive cross-immunity tests and showed the similarity between scrub typhus fever and tsutsugamushi disease by both intraocular and intradermal reactions in rabbits and monkeys. From cross-protection tests between the rickettsias of Samatran fever and the tsutsugamushi disease of British Malaya performed on monkeys and rabbits it appears that these diseases are identical. In addition to these reasons, it should be borne in mind that travel in those parts of the world is sufficiently great so that persons could easily be transported to those areas well within the period of communicability of this disease and infect the vector and animal reservoir.

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old theory that constipation is responsible. This ancient idea has been kept alive in modern times by equally vigorous advertising. There was no case in this series in which weakness or fatigue could be blamed on constipation. Although it may be true that some people have an increased sense of well-being with daily evacuation of the bowels, ill effects from so-called "poor elimination" have been tremendously exaggerated.

A sluggish liver has frequently been blamed for lack of energy, a charge of which this important

General weakness is generally blamed on a weak heart, but all cardiologists agree that this is not a frequent symptom of heart disease. In this series it occurred in only 8 cases (3 per cent). In the majority of cases, heart disease brings about other symptoms that cause the patient much more concern, such as dyspnea, pain in the chest and swelling of the feet. It should be pointed out that when a patient with a heart lesion complains only of weakness, this symptom is not likely to have any relation to the heart. In cases of neurocirculatory

ETIOLOGY

PHYSICAL DISORDERS IN 61 OF 300 CASES-20%

CHRONIC INFECTIONS	NUMBER	PERCENT	
• RESPIRATORY			
TUBERCULOUS	3		
NON-TUBERCULOUS	8	13	43
• URINARY	1		
• SYPHILITIC	1		
METABOLIC DISORDERS			
• DIABETES	8	12	40
• MYXEDEMA	4		
NEUROLOGIC DISORDERS			
• MYASTHENIA GRAVIS	4		
• NARCOLEPSY	8	16	53
• PSYCHOMOTOR EPILEPSY	3		
• POSTOPERATIVE BRAIN TUMOR	1		
HEART DISEASE	8	27	
ANEMIA			
• PERNICIOUS	1		
• HEMOLYTIC	1	5	17
• SECONDARY TO CANCER	1		
• NUTRITIONAL	1		
• LEUKEMIC	1		
NEPHRITIS	3	10	
MISCELLANEOUS			
• VITAMIN DEFICIENCY	1		
• LUNG TUMOR	1		
• HODGKIN'S DISEASE?	1	4	13
• UNCLASSIFIED FEVER	1		

FIGURE 2.

organ of the body is almost innocent. Even when hepatic disease has led to a breakdown in liver function, symptoms other than general weakness or

asthenia the patient may complain of weakness, but the chief complaint is oftener palpitation or dyspnea.

TABLE 1. Conditions Considered Frequent as a Cause of Weakness but Rarely Encountered.

CONDITION	ACTUAL INCIDENCE	
	NO. OF CASES	PERCENTAGE
Lay opinion		
Lack of vitamins	1	0.3
Poor elimination	0	0
Sluggish liver	0	0
Weak heart	8	2.7
Cancer	2	0.7
Medical opinion		
Anemia	5	1.7
Blood pressure	0	0
Thyroid disease	4	1.3
Adrenal deficiency	0	0
Pluriglandular disorders	0	0
Undulant fever	0	0

lack of energy are likely to appear. Yet it has been observed that patients who have had jaundice may continue to feel weak for many months afterward.

Cancer is frequently feared when chronic ill health of any kind appears, but it was found in only 2 cases (0.7 per cent). Cancer seldom causes weakness and exhaustion unless it is so far advanced that anemia or cachexia has resulted. Carcinoma of the cecum or ascending colon may lead to advanced anemia before other symptoms have attracted attention, but as a rule other symptoms precede and supersede in importance the complaint of weakness. With Hodgkin's disease, chronic ill health with lack of energy is often the dominant complaint.

CURRENT MEDICAL OPINION

A comparison of these actual observations with current medical opinion regarding the causes of weakness and fatigue also shows important differences.

THE DIFFERENTIAL DIAGNOSIS OF WEAKNESS AND FATIGUE*

FRANK N. ALLAN, M.D.†

BOSTON

ONE of the problems most frequently encountered by the general practitioner and the internist is a complaint variously described as weakness, exhaustion, fatigue, loss of ambition, low vitality or weak spells. Weakness and fatigue, alone or dominating a group of other symptoms, cause thousands of people to suffer disability and a greatly lessened enjoyment of life. What can the physician do to investigate these complaints and how can he determine their cause? To present an answer to this question from our experience at the Lahey Clinic, data have been compiled on 300 consecutive cases in which weakness, fatigue or weak spells were the chief complaint.

RESULTS

In 61 cases (20 per cent), the complaint was caused by a physical disorder (Fig. 1). In 239 cases (80 per cent), it was apparently not due to a physical disorder but was the result of a nervous state of one kind or another. Weakness due to hunger and fatigue caused by hard labor were not encountered. However widespread these conditions may be, they are not likely to bring the patient for medical attention.

Of the 61 cases in which a physical disorder was found to be the cause of weakness, it was possible in 28 cases to make the diagnosis by clinical observation alone, the history and physical findings pointing to the cause and nature of the disorder. In 20 cases, the disease was hidden and the diagnosis could not be made without laboratory tests or roentgenograms. Thirteen cases were on the borderline, and special laboratory work or roentgenograms were needed to confirm or disclose the diagnosis.

An analysis of the physical disorders causing weakness and fatigue represented by this series is shown in Figure 2. Chronic infections, including tuberculosis, and even more frequently nontuberculous pulmonary infection, sometimes in the convalescent period, were found in 13 of the 300 cases (4 per cent). Metabolic disorders were found in 12 cases (4 per cent)—8 of diabetes and 4 of myxedema. In 8 cases (3 per cent) there was heart disease. In 16 cases (5 per cent) there were neurologic disorders including 4 cases of *myasthenia gravis*, 8 of narcolepsy and 3 classified as psychomotor epilepsy. Anemia of different types was found in 5 cases. Miscellaneous causes accounted for the remaining 4 cases, including 1 each of carcinoma of the lung, vitamin deficiency, recurrent fever possibly due

to Hodgkin's disease and unclassified low-grade fever.

It should be noted that complex problems and unusual conditions are more likely to be seen in hospital or clinic work than in general medical practice. Furthermore, a relatively small series such as this one can give only the general trend of distribution of cases. A larger one would almost certainly

FINDINGS IN 300 CASES

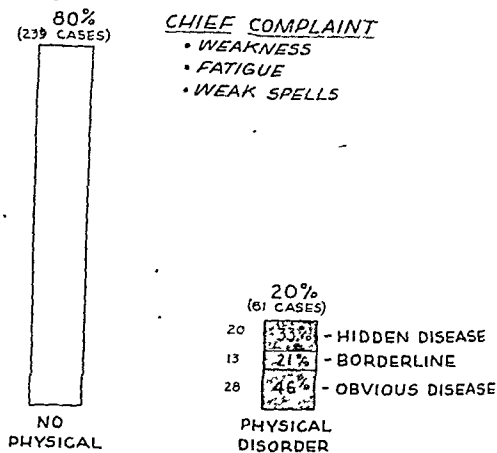


FIGURE 1.

include important disorders that were not present in this group, such as Addison's disease and subacute bacterial endocarditis. Yet these observations give a fair picture of what the physician may expect to encounter when consulted by a patient who complains of weakness.

CURRENT LAY OPINION

If these causal conditions are compared with those usually blamed for weakness and fatigue, a considerable deviation from current lay and medical opinion is noted (Table 1). In the minds of the public, lack of energy tends today to mean lack of vitamins. This idea has been exploited by the manufacturers of vitamin products. Our experience lends no support to the theory that vitamin deficiency seriously affects the health of a large percentage of the population. In this representative group of 300 cases there was only 1 in which vitamin deficiency was held responsible for weakness.

The concept of vitamin deficiency as a cause of lack of energy has now surpassed the still widely

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

†Co-director, Department of Internal Medicine, Lahey Clinic.

orning and decreases during the day; when days with excellent vigor are followed by days of exhaustion, with no change in activity to account for such a difference; when immediate benefit follows the use of a medication that has a slow pharmacologic action such as vitamins, thyroid, iron, liver extract and digitalis; when the weakness immediately returns on the omission of the customary treatment with these drugs for a single day; when the patient never has felt really well; when he has been tired and weak for over three years without

ing from benign forms of nervousness that were classified as chronic nervous exhaustion when extreme and simply as nervous fatigue when of milder degree (Fig. 3). The percentage of neurotic patients must be higher than actually exists in the general run of people who have these complaints, because such patients are much more likely than others to seek medical advice. It is important to distinguish the true neurosis from what may be called "benign nervousness," because the treatment must be planned differently (Table 2). A neurosis

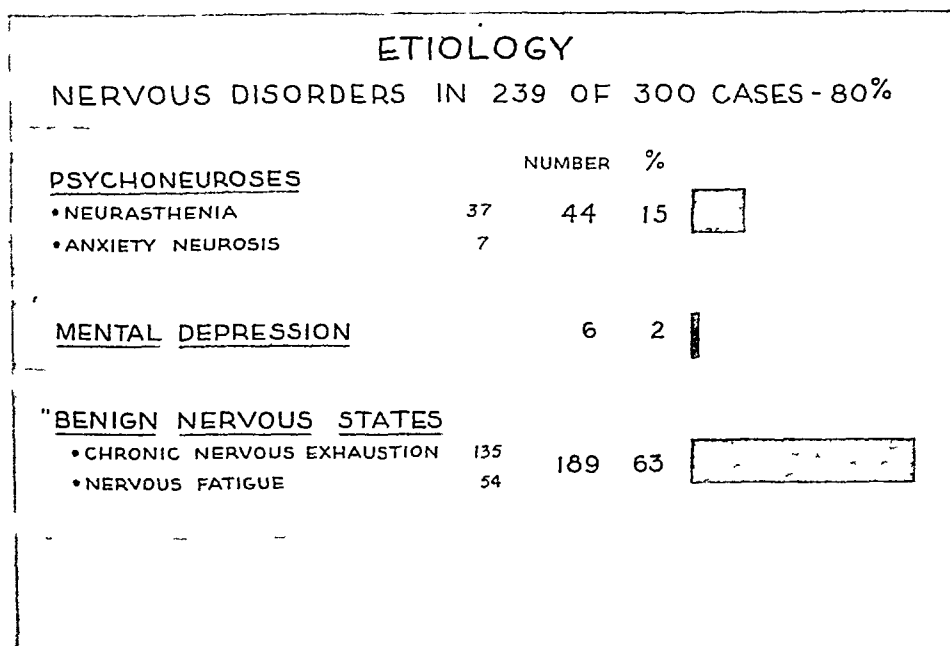


FIGURE 3.

evidence of a physical disorder; when he complains of nervousness, anxiety and worry and has symptoms that are obviously of nervous origin, such as a lump in the throat, tension in the back of the neck, difficulty in getting a satisfying breath or palpitation, when he denies a nervous state but reveals it by a multiplicity of complaints, variation in emphasis on different symptoms, vagueness of description and nervous behavior, such as flushing and weeping. One must give some attention also to a family history of nervous breakdowns and to a personal history of excessive nervous strain, but these should not be given so much weight as the other factors mentioned.

CLASSIFICATION OF NERVOUS STATES

There is need for discrimination in dealing with the nervous states responsible for weakness and fatigue. One should certainly not assume that any nervous condition represents a neurosis. Only one fifth of the patients with nervous disorders were frankly neurotic. The remainder were suffer-

ing from benign forms of nervousness that were classified as chronic nervous exhaustion when extreme and simply as nervous fatigue when of milder degree. The patient with the latter is born with a constitution no different from the average, but he comes to suffer from nervous fatigue or

TABLE 2. *Differential Diagnosis of Neurosis and "Benign Nervousness"*

DATUM	NEUROSIS	BENIGN NERVOUSNESS
Etiology	Largely intrinsic	Largely extrinsic
Background	Constitutional inadequacy	Average
Family history	Nervous breakdown (frequent)	Average
Multiple complaints	Usual	Unusual
History	Changeable	Consistent
Onset	Vague	Fairly definite
Duration	Often since childhood	Limited
Reaction to reassurance	Disappointment	Satisfaction

exhaustion because of special stress and strain, overwork, excessive worry or loss of sleep. If he is assured that the physical examination has shown no disorder, he expresses satisfaction. The reaction of the neurotic patient, on the other hand, is one of disappointment. He stresses the serious-

One finds *anemia* high on the list of conditions often treated for the complaint of weakness. It was found in only 5 cases (1.7 per cent). Attention is sometimes wrongly focused on minor deviations from the normal in the hemoglobin and red-cell count. Furthermore, the frequently used Tallqvist test for hemoglobin may give fallacious readings. In general, one may safely say that anemia does not cause weakness unless the hemoglobin drops below 70 per cent and the red-cell count well below 4,000,000.

A diagnosis of *low blood pressure* is often made when the blood-pressure readings are actually within normal range. Too much attention has been paid to possible ill effects of a systolic blood pressure below 110. Intensive treatment is often undertaken to raise it, and one finds expression of satisfaction because of a rise in pressure from 105 to 115. Perfect health and vigor are compatible with a systolic blood pressure as low as 90, and on the average the expectation of life is longer with the blood pressure at the lower range of normal. High blood pressure is sometimes also blamed for lack of energy, but when a hypertensive patient complains of lack of energy it is more likely to be due to increased nervous tension than to increased vascular tension. In none of these cases was weakness related to the blood pressure.

Myxedema was responsible for lack of energy in 4 patients (1 per cent), but this must be higher than the incidence in ordinary practice. A diagnosis of thyroid deficiency is often mistakenly made because the patient feels tired and looks fat and the basal metabolic rate is -15 or -20 per cent. Deviations from the standard rate may be found in many healthy people. A low basal metabolic rate not related to thyroid deficiency is seldom accompanied by any change in health, but there are a few patients who have diminished energy. The diagnosis of thyroid disease should not be made unless a low metabolic rate is accompanied by clinical evidence of the condition. If there is any doubt, a determination of the blood cholesterol level may aid the diagnosis more conclusively than does the basal metabolic rate. The blood cholesterol is almost invariably above normal in the presence of hypothyroidism; if one finds a low metabolism without high blood cholesterol, thyroid disease can usually be excluded.

Hyperthyroidism causes weakness, but it is seldom the chief complaint except in the severe long-standing cases and in the apathetic cases of old age.

Addison's disease is manifested by the most extreme weakness, but it is a rare disease. In far-advanced cases, the diagnosis readily is made from the clinical picture, including abnormal pigmentation, hypotension, gastrointestinal disturbances and loss of weight, in addition to the asthenia. In early or borderline cases the diagnosis may be aided by special tests. One of these, introduced by Kepler

and his co-workers,* is simple and easy to perform. The patient restricts his fluid intake and saves all the urine passed during the night for a period of nine hours. The following morning he is given four to six glasses of water (9 cc. per pound of body weight), and the excretion of urine is measured each hour for four hours. If the excretion in any one hour exceeds the total volume of urine excreted during the night, Addison's disease can be excluded. If there is a low excretion, Addison's disease may be present, but to rule out other conditions that may interfere with water balance, further study is needed.

Other *endocrine conditions*, especially pluriglandular disorders, are often blamed for fatigue. There is seldom any sound basis for the diagnosis, although in a few cases of pituitary tumor lack of energy is indeed an early sign.

Undulant fever is currently given a great deal of attention in certain parts of North America. It must be considered in any case of long-continued fever or ill health, but the diagnosis should not be made on insufficient evidence. Positive agglutination reactions, unless in a high titer, and positive skin tests should not alone decide the diagnosis. In the absence of a history of acute or subacute febrile illness some time in the course of the disorder, the diagnosis is open to question.

DIAGNOSTIC STUDIES

Investigation of the complaint of weakness, fatigue or lack of energy must begin with a review of the history from every standpoint. Patients often fail to mention even significant symptoms. The detailed history must be followed by a careful physical examination. The history and examination should enable one to make a complete diagnosis in about half the cases in which a physical disorder is responsible for the complaint. It should also enable one to suspect hidden or practically hidden disease and should furnish clues to the complete diagnosis.

It is often assumed that the diagnosis of a nervous state must be deferred until the examination, laboratory tests and roentgenograms have ruled out a physical cause for the complaint. This is the wrong point of view. The diagnosis of a nervous state should be made by direct observation of the characteristics of such condition and not be reached entirely by exclusion. If the patient has a physical disorder and a nervous state, they must both be recognized and evaluated in order to make a complete diagnosis and to undertake effective treatment.

CHARACTERISTICS OF NERVOUS STATES

One must suspect that weakness and fatigue are due to a nervous state under the following circumstances: when the lack of energy is greatest in the

*Robinson, F. J., Power, M. H., and Kepler, E. J. Two new procedures to assist in recognition and exclusion of Addison's disease. *Proc. Staff Meet., Mayo Clin.* 16:577-583, 1941.

morning and decreases during the day; when days with excellent vigor are followed by days of exhaustion, with no change in activity to account for such a difference; when immediate benefit follows the use of a medication that has a slow pharmacologic action such as vitamins, thyroid, iron, liver extract and digitalis; when the weakness immediately returns on the omission of the customary treatment with these drugs for a single day; when the patient never has felt really well; when he has been tired and weak for over three years without

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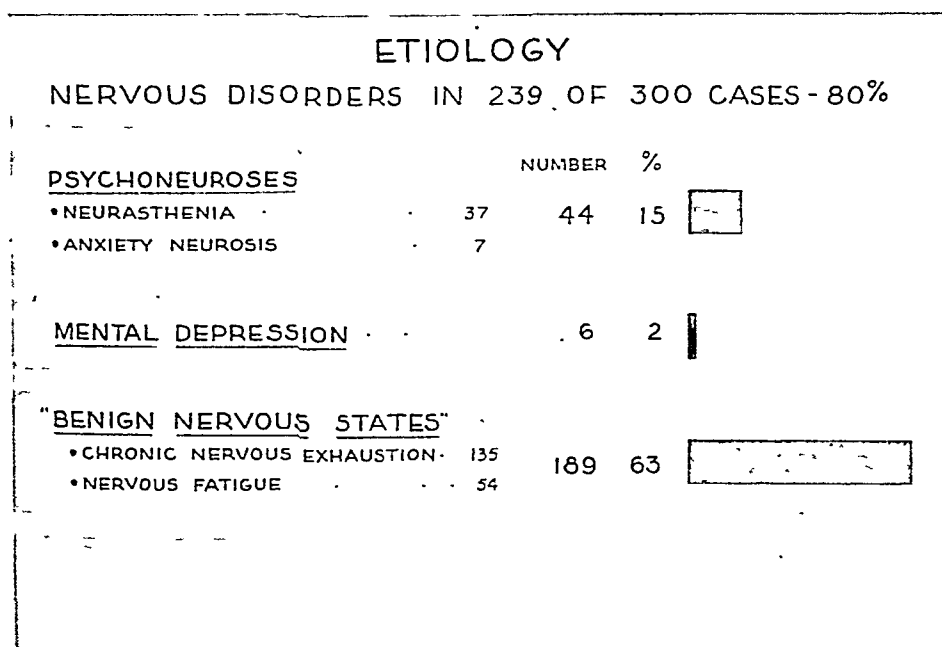


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is largely dependent on intrinsic factors, whereas a benign nervous state is largely dependent on extrinsic factors. The patient with the latter is born with a constitution no different from the average, but he comes to suffer from nervous fatigue or

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ing from exhaustion because of special stress and strain, overwork, excessive worry or loss of sleep. If he is assured that the physical examination has shown no disorder, he expresses satisfaction. The reaction of the neurotic patient, on the other hand, is one of disappointment. He stresses the serious-

ness of his complaints and insists that some abnormality must be found to account for them.

DIAGNOSTIC PROCEDURES TO IDENTIFY PHYSICAL DISORDERS

To make a complete search for physical disorders, various methods of investigation may be undertaken. These should include in all cases urinalysis and the usual blood tests, such as the red-cell and white-cell counts, examination of the blood smear, determination of the hemoglobin and the Hinton, Wassermann or other test for syphilis. The routine urinalysis may lead to the discovery of diabetes, which can be recognized in no other way. In about half the cases of diabetes seen at the Lahey Clinic, typical diabetic symptoms and complications are absent. The urinalysis may also reveal nephritis and pyelitis. The blood test may disclose primary blood disorders and changes secondary to systemic infection or other disease.

A roentgenogram of the chest is obligatory for all young people who feel tired and for people of any age who have a past history of pleurisy, contact with tuberculosis or respiratory symptoms such as cough. If any hidden infection is suspected, a daily record of the body temperature should be kept for three days or more. The blood-sedimentation rate should be determined, and also the agglutination test for undulant fever when the past history suggests the possibility of infection of this type. Blood-sugar tests should be made when the relation of symptoms to lack of food and to exertion arouses suspicion of hypoglycemia. The basal metabolic rate and the blood cholesterol test aid in the diagnosis of weakness due to thyroid disease, the adrenal-function test of Kepler and his co-workers in cases of suspected Addison's disease, and roentgenograms of the head in detecting enlargement of the sella in cases of tumor of the pituitary gland.

Laboratory tests for vitamin deficiency have not received widespread clinical application. As a

rule, a therapeutic test is the best support now available for the clinical diagnosis of hypovitaminosis, although far too often the results are not subject to a control test.

In the neurologic field the prostigmine and quinine tests for myasthenia gravis and the electroencephalogram are available.

CONCLUSIONS

In a series of 300 cases in which medical examination was requested because of weakness, fatigue and weak spells, the complaint was found to be caused by a physical disorder in 20 per cent. In the remainder the complaint was not caused by any physical disturbance but was the result of a nervous state. This was classified as a neurosis in approximately 20 per cent, and as a benign nervous state, chronic nervous exhaustion or nervous fatigue in the rest of the cases.

In nearly half of the cases in which a physical disorder was found to be the cause of weakness, it was possible to make a positive diagnosis by clinical observation alone. In the others, laboratory tests or roentgenograms were essential to reveal a hidden disease or confirm the diagnosis. The most frequent physical disorders were chronic infection, diabetes, heart disease, various neurologic disorders and serious diseases of the blood. Certain conditions, such as vitamin deficiency and glandular disorders, considered widespread causes of weakness by both the laity and the medical profession, were actually found to be rare, and not a single case of weakness due to liver trouble, poor elimination or low blood pressure was encountered.

The study of weakness and fatigue leads to a consideration of medical problems covering almost every field of medicine. Although a high percentage of patients with these complaints have no physical disorder, there is a group in which physical conditions of unusual interest may be discovered. In any case these symptoms warrant thorough and complete investigation.

605 Commonwealth Avenue

EXTRARENAL TUBERCULOUS LESIONS ASSOCIATED WITH RENAL TUBERCULOSIS

DAVID S. CRISTOL, M.D.,* AND LAURENCE F. GREENE, M.D.†

ROCHESTER, MINNESOTA

RENAL tuberculosis is too often symptomatically silent during the time when it can be treated most successfully. Although the diagnosis of this condition can be made most satisfactorily by the identification of the organism in the urine and can be confirmed by inoculation of laboratory animals, in many cases the disease escapes recognition in its early stages simply because tuberculous infection is not suspected. Hence any symptom, sign or roentgenographic or laboratory finding that may cause one to suspect the diagnosis of renal tuberculosis is worthy of investigation or evaluation.

CALCIFIED MESENTERIC LYMPH NODES

Calcified mesenteric lymph nodes are seen frequently in the routine roentgenograms of the urinary tract. They usually attract attention only when they are so situated as to make it necessary for them to be distinguished from urinary calculi. This is only rarely essential. Although there are several conditions believed to be responsible for the pathologic change in the lymph nodes that is followed by calcification, the vast majority of calcified mesenteric lymph nodes have been the seat of tuberculous infection. This fact prompted us to study the incidence of calcified mesenteric lymph nodes in cases of proved renal tuberculosis. To accomplish this, we carefully examined the intravenous urograms and retrograde pyelograms in 145 consecutive cases of proved renal tuberculosis, in each of which nephrectomy had been performed, so that hence a pathological as well as a bacteriologic diagnosis had been made. This series was compared with a series of 145 consecutive cases of surgically treated renal

TABLE 1. Incidence of Calcified Mesenteric Lymph Nodes in Cases of Renal Tuberculosis and of Nontuberculous Renal Lithiasis

PATIENTS	RENAL TUBERCULOSIS		NONTUBERCULOUS KIDNEYS	
	NO. OF CASES	PERCENTAGE	NO. OF CASES	PERCENTAGE
Men	81		93	
With calcified mesenteric lymph nodes	8	10	3	3
Women:	64		52	
With calcified mesenteric lymph nodes	11	17	5	10
Totals	145		145	
Percentages		13		6

lithiasis in many of which nephrectomy was performed and in each of which the diagnosis of renal tuberculosis was excluded.

Table 1 shows the incidence of calcified mesenteric lymph nodes in both series of cases. Calcified

mesenteric lymph nodes were found to be present in 13 per cent of the roentgenograms of patients suffering from proved renal tuberculosis. This incidence was more than twice that found in a comparable series of patients not suffering from renal tuberculosis.

TUBERCULOUS EPIDIDYMITIS

Although it is generally known that renal tuberculosis is fairly frequently accompanied by genital tuberculosis, too often intractable epididymitis is treated for long periods before the kidneys are investigated.

In 34 (42 per cent) of the 81 male cases of proved renal tuberculosis incorporated in the preceding study, genital tuberculosis also was present (Table 2). None of the 93 male subjects in the control group suffered from inflammation of the genitalia.

TABLE 2. Incidence of Tuberculous Epididymitis and Prostatitis in Cases of Renal Tuberculosis and of Nontuberculous Renal Lithiasis.

GENITAL INVOLVEMENT	RENAL TUBERCULOSIS		NONTUBERCULOUS KIDNEYS	
	NO. OF CASES	PERCENTAGE	NO. OF CASES	PERCENTAGE
Tuberculous epididymitis	31	38	0	0
Tuberculous prostatitis	3	4	0	0
None	47	58	93	100
Totals	81		93	

Thirty-one of the 34 patients had proved tuberculous epididymitis, and the remaining 3 were believed to have tuberculous prostatitis. In 15 of these cases it was necessary to remove the kidney on the same side as the involved epididymis, and in 7 cases the kidney on the opposite side from the involved epididymis was removed. In 9 cases both epididymides were involved.

The frequency of concomitant genital and renal tuberculosis is so great that the genitalia of every male patient complaining of urinary symptoms should be carefully examined for evidence of tuberculosis. Although renal tuberculosis frequently occurs in the absence of genital tuberculosis, the latter is accompanied more often than not by renal tuberculosis. Every male patient who has epididymitis of possibly tuberculous nature should therefore receive complete urologic investigation, even in the absence of urinary symptoms. In this manner the early renal lesions of tuberculosis may be detected.

PULMONARY TUBERCULOSIS

Since we share the general opinion that renal tuberculosis largely if not entirely represents a

*Fellow in urology, Mayo Foundation.

†Instructor in urology, Mayo Foundation; member, Section on Urology, Mayo Clinic

secondary hematogenous focus of tuberculous activity resulting from a primary pulmonary infection, we decided to investigate the incidence of pulmonary involvement in these 290 cases. To do this we reviewed the pulmonary roentgenograms of the 145 proved renal tuberculous patients and the 145 control patients suffering from operative renal lithiasis. As shown in Table 3, each case was relegated to one of three categories: first, the healed

TABLE 3. *Incidence of Pulmonary Tuberculosis in Cases of Renal Tuberculosis and of Nontuberculous Renal Lithiasis.*

THORACIC INVOLVEMENT	RENAL TUBERCULOSIS		NONTUBERCULOUS KIDNEYS	
	NO. OF CASES	PERCENT-AGE	NO. OF CASES	PERCENT-AGE
Healed or active adult type	50	34	6	4
Healed childhood type (Ghon complex)	20	14	20	14
None	75	52	119	82
Totals	145		145	

or active adult type of tuberculosis; second, the healed childhood type of tuberculous infection, which often is referred to as the Ghon complex; and finally, those cases not showing any pulmonary pathologic change whatsoever, which were designated as negative.

The findings clearly demonstrate the frequency with which renal tuberculosis is associated with healed or active adult-type pulmonary tuberculosis. It is of incidental interest that the frequency of the healed childhood type of tuberculosis was the same in the two series.

SUMMARY AND CONCLUSIONS

The diagnosis of renal tuberculosis can be established relatively easily once this disease is suspected. Too frequently this condition, whose successful treatment depends on its early diagnosis, is not considered. The incidences of three easily demonstrable tuberculous lesions that are associated with renal tuberculosis have been determined. The presence of either of these associated conditions should cause one at least to suspect renal tuberculosis.

Since roentgenographically evident calcified mesenteric lymph nodes are more than twice as frequent in cases of proved renal tuberculosis as in a control nontuberculous group of patients, the presence of calcified mesenteric lymph nodes in the roentgenogram of a patient suffering from a urologic disease should cause one to consider the diagnosis of renal tuberculosis.

Since epididymitis occurred in 38 per cent of 81 cases of renal tuberculosis but did not occur in a control group of 93 cases, every case of intractable epididymitis should be considered tuberculous until proved otherwise. The condition of the kidneys of such a patient should be promptly evaluated.

Since roentgenographic evidence of healed or active adult type of pulmonary tuberculosis is more than eight times as frequent in cases of renal tuberculosis as in a comparable control group, in every case of renal tuberculosis the patient should have the benefit of a stereoroentgenogram of the thorax. Furthermore, renal tuberculosis should be excluded in any case of pulmonary tuberculosis in which there are subjective or objective urinary findings.

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MEDICAL PROGRESS

MODERN CONCEPTS OF RENAL STRUCTURE AND FUNCTION IN CHRONIC BRIGHT'S DISEASE*

STANLEY E. BRADLEY, M.D.†

BOSTON

DURING recent years an intensive application of well-established methods of micromorphology has broadened considerably the knowledge of the anatomic patterns of renal disease. Likewise, great strides have been made toward an understanding of renal pathologic physiology through the development of new functional tests. These two avenues of approach have converged on the central problem of the relation between renal structure and function, and when integrated, allow insight into some of the more remote physiologic disorders and clinical manifestations of renal disease. It is the purpose of this review to discuss recent advances in the pathology and physiology of the kidneys as affected by the various forms of Bright's disease.

STRUCTURE

Factors capable of deforming the architecture of the kidney include vascular disturbances, interstitial tissue proliferation and nephron damage. The last may be secondary to the direct action of noxious agents, to ischemia, to blockage by casts and to the mechanical effects of scar tissue. These factors operate to some extent in all forms of chronic renal disease at a tempo depending on the nature of the primary process, so that each type of disorder is characterized by a distinctive pathology of structure and function, at least early in the course of the disease. In the terminal stages, however, there is a tendency to develop a final common pattern, probably because the same fundamental processes are active in all. Clinically, also, the terminal picture in all forms of Bright's disease is similar.

Vasculature

Vascular changes play a prominent role in the disorganization of renal anatomy. Vascular rearrangement of itself necessarily causes architectural disorder with resulting disturbances in blood supply that directly affect the parenchyma. In all forms of chronic renal disease, the vascular pathology appears to be fundamentally similar but the extent to which it dominates the picture depends on the etiology. In the kidney of essential hypertension it is of prime importance; in glomerulonephritis it is

of considerably less importance; and in certain nephroses it is, at first, apparently of little or no importance. In all, however, with time and progression, vascular alterations occur and probably contribute to further damage.

The unique circulatory pattern of the kidney is such that interference with the flow of blood through the glomerulus would be expected to disturb the flow through the peritubular capillaries and cause damage to the attached tubule. This surmise has been supported by the finding that direct communications between the interlobular or arcuate arteries and the peritubular capillaries are absent, or at least exceptional, in the normal kidney.¹ Thus it has seemed reasonable to explain tubular damage in glomerulonephritis and nephrosclerosis on the basis of glomerular obstruction and the resultant ischemia and atrophy of the attached tubule.² Recently, however, in aged persons many direct arterial communications with the postglomerular circulation have been found,¹ and in chronic renal disease it has been shown that glomerular patency is not necessary for an efficient circulation of blood through the peritubular capillaries.³⁻⁵

Oliver and his co-workers³ have demonstrated that direct arterial connections with the peritubular capillaries appear in larger and larger numbers as glomerular damage increases. These communications spring from the arcuate and interlobular arteries and from the afferent arterioles. The latter types appear to be of special importance. First observed by Isaacs in this country and later by Ludwig, they have come to be called Isaacs-Ludwig arterioles or simply Ludwig's vessels.⁶ A Ludwig vessel comes off the afferent arteriole perpendicularly or obtusely and straightway enters the tubular capillaries by-passing the glomerulus. Preceding the development of this collateral circulation there is thickening of the basement membrane, proliferation of extracapillary connective tissue and capillary endothelium and an occlusion of glomerular capillary loops.³ Additional obstruction to flow of blood through the glomeruli has been attributed to deformation of the corpuscle by the overgrowth of interstitial elements, and by hypertrophic or hydronephrotic tubules.³ When amyloidosis is the cause of chronic renal disease, amyloid material may be found about the cells of the subintimal layers,⁷ at first in discrete deposits, which later coalesce to produce rigidity and luminal narrowing and, in

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Instructor, Department of Medicine, Boston University School of Medicine; assistant physician, Evans Memorial, Massachusetts Memorial Hospitals.

the glomerulus, occlusion of the loops. In addition, the capillary networks become thicker and the large vessels are more sharply defined by parietal changes, until the parenchyma of the kidney seems to rest upon a scaffolding of numerous relatively rigid vessels.⁸ In all types of chronic renal disease intimal thickening and deposits of lipoidal material contribute to vascular rigidity. Vessels may be formed *de novo* but mainly seem to be derived from pre-existing channels. Thus, after infarction the newly appearing collateral vessels arise largely from a remodeling of those already present.⁹ Spanner¹⁰

doubt that certain unusual cells appear among the myocytes in the media of renal arteries and arterioles and are particularly numerous close to the junction of the afferent arterioles and the malpighian corpuscles in mice, rats, dogs, cats, rabbits, ferrets and man.¹¹ They are, however, variously described, and it is questionable whether they are identical structures in the various species and whether more than one type occurs. Close to the glomerulus (Fig. 1) the internal elastic membrane may disappear and the media may be replaced by a thick sheath of cells, somewhat larger than myocytes,

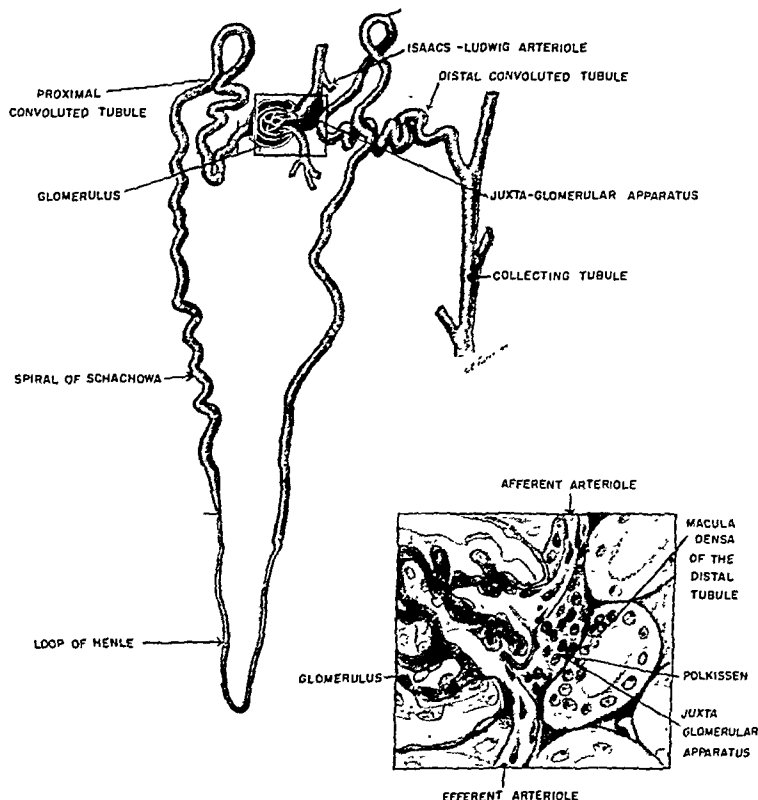


FIGURE 1. Schematic Representation of a Typical Human Nephron Showing the Important Structures.

The juxtaglomerular apparatus and the macula densa of the distal tubule are shown in greater detail at the lower right.

has demonstrated arteriovenous anastomoses anatomically in the human kidney, and it has been suggested that retrograde perfusion of the peritubular capillaries through these structures may follow glomerular obstruction. Activity of these anastomoses, however, has not been observed in chronic disease,³ and they appear to be completely lacking in infarcted areas.⁹

Juxtaglomerular Apparatus

Interpretation of the histologic structure of the afferent arteriole remains as confused as it was when Smith⁶ reviewed the subject at some length in his Harvey Lecture of 1939. There seems to be little

that have a clear cytoplasm in which acidophilic granules may or may not be found. In the human kidney these granules may be fluorescent.¹² The cuff pouts out eccentrically at the point of junction with the capsule to form a polar pad (*Polkissen*) closely attached to a segment of the distal convoluted tubule. The distal tubular segment at this point shows crowding and increased height of the epithelial cells, the macula densa. The argument concerning the identity of the medial cells appears to revolve about the presence and character of granules that were absent in the cells of the *Polkissen* described by Zimmermann¹³ but present in the "epithelioid cells" described in the media by Ruyter,¹⁴ Oberling¹⁵

and Goormaghtigh¹⁶; they are large and striking in the mouse but small and inconspicuous in man. After further study this conflict may be resolved on the basis of the differences in species and of the various histologic methods employed. A number of workers have been struck by the resemblance of these cells to the "epithelioid cells" that invest the vessels in the normal glomus and appear so strikingly in glomus tumors.¹⁷ It is usually stated that these cells have a clear cytoplasm. Zimmermann¹⁸ denies that the cells observed by him were epithelioid in character and observed fine fibers that passed through the cytoplasm. He did, however, describe "pericytes" about the glomerular capillaries — cells apparently derived from the smooth muscle and capable elsewhere in the body of regulating capillary flow. Murray and Stout¹⁷ have recently shown that epithelioid cells from glomus tumors take on, in tissue culture, all the characteristics of the typical pericytes of Zimmermann. Hence, the possibility remains that the cells in question represent an intergrade in the transition between the smooth-muscle cells of the media of the afferent arteriole and the pericyte of the glomerular capillaries.

Goormaghtigh¹⁶ has named the structure at the terminus of the afferent arteriole the "myoneuro-arterial juxtaglomerular apparatus." Its description is germane to the present discussion because of the view expressed by Goormaghtigh^{18, 19} and others^{20, 21} that the structure is an endocrine organ, the probable site of renin formation. Opposed to this is the notion, based on the resemblance of the structure to glomic cells found at arteriovenous anastomoses in the digits and elsewhere, that it regulates the flow of blood through the glomerulus in response to nervous stimulation of the thick neural net associated with it, and to chemical stimulation of the macula densa by the urinary constituents.^{15, 22} The first hypothesis is supported by the finding of Goormaghtigh and Grimson,²³ confirmed by Graef,^{6, 11} that hypertrophy of the structure occurs during experimental renal hypertension and by their further finding, confirmed by others,^{20, 21} that hypertrophy of this structure occurs in essential hypertension, nephritis and eclampsia. Oberling,²² however, failed to find such hypertrophy frequent in hypertension but, on the contrary, noted degeneration and regression. He believes that the lesions described by Goormaghtigh are the result of hypertension and represent muscular hypertrophy and arteriosclerosis. Moreover, such hypertrophy is usually not striking or uniform, and it is an admittedly uncommon finding.¹⁰ The second suggestion lacks any supporting evidence, although an abundant innervation of the structure has been demonstrated.

Recently a singular case was reported by Graef²⁴ in which hypertrophy of afferent arteriolar medial cells presented the only pathological evidence of renal disease. The patient, a woman of thirty,

suffered from hematuria, proved to be unilateral. In the third month of pregnancy nephrectomy was performed on the basis of a diagnosis of renal neoplasm. The excised kidney appeared grossly normal, but microscopic examination revealed a striking change in all the arterioles, consisting of hypertrophy and hyperplasia of the medial cells with luminal constriction. These changes were especially marked at the point of entrance of the afferent arteriole into the glomerular network, where the hypertrophic changes were so extensive as to indent the glomerulus and surrounding tubules. All the cells were granular, and the cytoplasm was quite clear. Erosion of the pelvic and ureteral epithelium appeared to account for the hematuria. The subsequent course of this patient was of significance, for after an uneventful postoperative recovery, toxemia of pregnancy appeared in the ninth month of gestation, with proteinuria, hypertension, convulsions and coma. Recovery followed spontaneous delivery of a stillborn child. Hypertension continued to be present during the succeeding month and then the blood pressure returned to normal. Graef suggests that hormonal activity during pregnancy may be responsible for a change in vascular smooth muscle similar to the change in the myometrium.

Interstitium

In all forms of Bright's disease, active and passive alteration of the renal interstitial tissue is prominent. The disappearance of nephrons creates dead space filled by connective tissue, usually with thickening of the stroma by shrinkage rather than by proliferation. In addition to this passive increase in stroma there may be an active process of fibrous-tissue proliferation, probably in a large part secondary to inflammation, evident pathologically by the cellular infiltration. This is most profound in pyelonephritis or, as Bell²⁵ calls it, "exudative interstitial nephritis," where bacteria may be found exciting an inflammatory response to the point of abscess formation with sequential fibrous-tissue proliferation.²⁶ In glomerulonephritis, inflammatory changes ranging from edema and polymorphonuclear infiltration to fibroblastic proliferation with collagen formation and round-cell infiltration may be observed.³ The normally thin sheets of fibrous tissue are widened to thick bands, which may at first increase the bulk of the organ but later cause shrinkage by destruction of the nephrons. The fibrillae are obviously newly added for they are irregular and disoriented and soon enmesh tubules and glomeruli, producing by constriction all degrees of atrophy and distortion.³ It seems clear that here, as in pyelonephritis, the interstitial inflammatory reaction precedes any serious modification of the renal parenchyma. In the kidney of the hypertensive, however, where vascular changes are predominant early in the course of the disease, the in-

terstitial modification is fairly simple and is mainly secondary to parenchymal shrinkage, with approximation of fibrils causing increased density.³ Inflammation is seen frequently enough, however, in the hypertensive kidney to sustain the belief that here, too, it contributes to the interstitial disorder.^{3, 27} Terminally, in all, if the course is protracted, granulations of the surface appear where connective tissue collapses and contracts about still viable nephric units, which may be greatly hypertrophied, while the kidney becomes small and misshapen.

Parenchyma

The three dimensional reconstructions of renal micromorphology in Oliver's laboratory³ have thrown new light on nephron structure in disease. It has been shown that pathologic nephrons may be broadly divided into two categories, the atrophic and the hypertrophic.²⁸ The *hypertrophic* nephron shows a striking change, almost entirely limited to the proximal tubules, which may be increased in bulk as much as ten times the normal. Cellular hyperplasia, luminal dilatation and increased length, especially marked in the terminal broad segment, the so-called "spiral of Schachowa," with displacement of Henle's loop, account for the increase in size. The distal tubule may be normal or may show evidences of other types of pathologic change. The *atrophic* nephron exhibits an irregular diminution in the size and number of the tubular cells. This may be associated with dilatation or stenosis. Of course, there is a considerable degree of intergrading so that hypertrophy and atrophy may appear side by side in the course traced by the tubule through the kidney, or the degenerative change may be so extreme as to lead to destruction of the walls and fragmentation of the tubule. Disruption often occurs close to the glomerulus in the proximal convoluted tubule and is followed by healing with the formation of aglomerular nephrons and atubular glomeruli. Either may persist long after the remainder of the unit to which it was formerly attached has completely disappeared. The aglomerular tubule may be otherwise entirely intact and show all the possible changes of atrophy and hypertrophy. Fragmentation may result in the formation of islets of tubular tissue that appear as clusters of cells or, more frequently, as small cysts filled with hyaline material.³

Vascular pathology and interstitial tissue proliferation are major causes of the lesions, but other factors may be equally important. Agents capable of both damaging and stimulating the renal parenchyma may manifest themselves by decreases in mitochondria,²⁹ deposits of lipoidal material, cloudy swelling and even severer changes leading to cell death on the one hand and by increases in nuclei and hypertrophy of cells on the other. Many of

these cellular changes may precede significant ischemia or fibrosis. It is probable that unidentified toxins are concerned in glomerulonephritis, pyelonephritis and certain of the nephroses. To what extent associated endocrinopathies may contribute to this is unknown. It is certain, however, that the appearance of large amounts of protein in the glomerular filtrate is accompanied by intracellular deposits of hyaline and lipoid material. Evidence based on chemical and electrophoretic studies of urinary protein suggests that the beta-globulin fraction of the plasma protein is largely responsible for the formation of hyaline casts and blockage of the tubules both in nephritis and in the renal failure of multiple myeloma.³⁰⁻³²

Intratubular casts that occlude the lumens and cause hydronephrotic changes cannot be neglected as a potent cause of tubule alteration.³ Almost the total length of a tubule may be filled with solid substance. These consolidated masses seem to be clearly ante mortem in origin and not artifacts. Casts are usually heterogeneous conglomerates of solid material, granular or hyaline in appearance, probably derived from precipitated constituents of the glomerular filtrate and desquamated tubular epithelial cells; many contain red cells and leukocytes. In pyelonephritis the tubules are frequently packed with leukocytes enmeshed in a hyaline matrix.²⁶ Later the leukocytes disappear and many tubules, cyst-like in appearance, remain blocked with a bluish-staining colloid material. It is stated that such casts are distinctive and diagnostic of pyelonephritis.³³ Casts are found in the collecting tubules and distal convoluted segments, and granular material is occasionally seen in the loop of Henle, but the proximal segment usually remains empty. This finding is in accord with the view that concentration of the glomerular filtrate takes place in the distal tubule. Whether primary blockage occurs in the collecting tubules, — which are characteristically affected by the disease, causing kinking and coiling to trap the solid material, — or in the distal tubule is not settled, but it seems likely that, although it occurs more frequently in the former, than in the latter, obstruction of the distal tubules can occur.³ Above the point of obstruction the tubule may dilate widely, and this dilatation may extend the full length of the tubule proximal to the block. The degree of structural alteration depends largely on the state of the stroma, which by constriction may cause the formation of varices, outpouchings or stenosis of the hydronephrotic tubules. The blocking cast may so fill out the distal segment as to encroach on and deform surrounding structures. The proximal convoluted tubule placed in close proximity to the distal segment may then be flattened to a ribbon, and the glomerulus, attached to the macula densa of the distal segment, may also be badly misshapen. The glomerulus is never dilated

the hydronephrosis of tubular blockage. This has also been shown to be the case in the normal kidney deformed by hydronephrosis.³⁴

* * *

Several important facts, therefore, have emerged from the recent studies of renal pathology, especially those of Oliver, whose monograph³ should be consulted for further detail. First, the doctrine of glomerular dominance of the renal circulation is discredited by the finding of a gradual development of a predominantly tubular circulation through accessory vascular channels. Second, the role of the interstitial tissue in the renal deformation of chronic Bright's disease is reaffirmed and established. Third, hydronephrosis secondary to the obstruction of nephrons and collecting tubules is emphasized as contributing to the architectural deformity. Finally, the demonstration of hypertrophic units and of aglomerular tubules raises the question of the functional ability of these structures.

It seems reasonable to infer that hypertrophy and hyperplasia of renal structures indicate adaptive functional responses to increased demands resulting from a shrinkage in the total functional mass. Likewise, similar changes in aglomerular nephrons seem to indicate continued activity requiring secretion of water across the tubular epithelium. Since it is known that, in certain fish, aglomerular kidneys secrete urine, it has been suggested by Marshall³⁵ that a return to the more primitive state may occur in chronic renal disease. The demonstration of an increasing number of intact aglomerular nephrons in the kidney of Bright's disease³ appears to substantiate this hypothesis. Functional evidence of the operation of such aglomerular units, however, is totally lacking.

Initial Patterns of Disease

Although the fact that all forms of Bright's disease converge on a common terminal pattern requires emphasis, it should be remembered that each form of the disease has a distinctive initial pattern. In glomerulonephritis, glomerular damage dominates the earliest stage. Endothelial proliferation blocks the glomerular capillaries, and thrombosis and occlusion by crescent formation are occasionally observed. Thickening, fusion and splitting of the basement membrane are followed by the appearance of intracapillary fibers. A widespread interstitial inflammatory reaction, an irregular dilatation of proximal tubules and occasionally small deposits of lipid material in the tubular cells or in the vessel walls may be found. If healing occurs, these evidences of disease may be entirely removed, but if activity continues, the structural alteration usually becomes profound within one or two years. Oliver³ is of the opinion that two types of chronicity are manifest. In one, atrophy, hydronephrotic dilatation and disruption of tubules, and glomerular

obliteration are predominant; in the other, extensive tubular hypertrophy and hyperplasia with vascular readjustments occur. He attributes the former to a continuously active disease process, and the latter to remittent activity of the disease process, during which recuperation and compensatory renal changes take place.

In the nephrosclerotic kidney is found a very different pattern, consisting of arterial and arteriolar sclerosis and little interstitial inflammation. The small arterial branches are always the more severely involved, showing tortuosity and fatty deposits in the walls. Hyperplasia of the endothelium is frequently seen in small arteries and large arterioles and is usually "associated with medial degeneration (intracellular collagen and thinning) and in many instances complicated by hyaline, fat, mucoid or chromotropic degeneration, or necrosis of the hyperplastic intima as well as of the media."³⁷ Hyalinization of the afferent arteriolar intima often occurs. Interstitial fibrosis is evidenced at first by the formation of a few scars; later it is diffuse, with the destruction of the greater part of the cortical tissue. The tubules show atrophic changes within the scar and hypertrophy outside it. In the accelerated form of the disease (malignant nephrosclerosis), extensive and complete occlusion of the tubules and marked hydronephrotic changes are widespread. In addition, variable changes in any one nephron, such as hypertrophy and atrophy, are of common occurrence. Necrosis of the wall of the afferent arteriole may be found, with contiguous inflammation of the surrounding interstitium.²⁷

The nephrotic kidney shows relatively little change in its architecture, even though numerous casts may fill the tubules and disruption may occur. Depending on the etiology a heavy lipoidal deposit in the tubular epithelium may be found.

In acute pyelonephritis, focal accumulations of polymorphonuclear leukocytes appear throughout the kidney, about venules and capillaries plugged by bacterial emboli or about glomeruli.^{25, 26} These accumulations may develop into multiple abscesses destroying and replacing local structures. Following release of the obstruction to urine flow in the experimental animal, and possibly in man, regression occurs, the lesions are resolved and a diffuse interstitial fibrosis sets in, which damages nephric units not previously affected by the disease.

Terminus and Differential Diagnosis

It is not unusual for renal disease to become clinically manifest only when the kidney fails, and it is precisely at this stage that differential diagnosis is particularly difficult because few distinctive pathological or clinical features may stand out. Since the processes involved in the disorganization of renal structure are common to all types of Bright's disease, it is not surprising that convergence from initially specific patterns on a terminal similarity

of structure and function occurs. Mansfield, Mallory and Ellis³⁸ have considered this problem in 59 patients dying in uremia at the Boston City Hospital in whom the diagnosis was made on pathological grounds. In these cases no pathognomonic pattern of clinical or laboratory findings could be discerned. It was thought, however, that a diagnosis should be attempted although frequently it could be reliably based only on a knowledge of the natural history of the disease. In many cases this information may be lacking and diagnosis must be tentative. Pathological diagnosis is usually less difficult but even then differentiation may be controversial. These facts are evident in the confusion in the literature regarding pathological differentiation of chronic and healed pyelonephritis from the other forms of chronic Bright's disease. Mansfield and his co-workers³⁸ quote unpublished data of Kinney and Mallory as indicating evidence of healed pyelonephritis in almost 14 per cent of all autopsies. On the contrary, Shure³⁹ found pyelonephritis in only 2.44 per cent (290 cases) of 11,898 post-mortem examinations and Bell²⁵ records an incidence of 2.47 per cent (808 cases) in 32,360 autopsies, of which only 64 cases were nonobstructive in origin. The great discrepancy in these figures can be attributed in part to a failure to establish uniform standards of diagnosis. Bell²⁵ and others^{40, 41} who have recently reviewed the literature reject pyelonephritis as an important cause of hypertension. Further studies are necessary to determine the relative importance of pyelonephritis and of chronic diffuse glomerulonephritis in causing renal failure.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 30381

PRESENTATION OF CASE

A forty-nine-year-old housewife entered the hospital because of jaundice.

The patient was in apparent good health until about one and a half years before admission, when she had an attack of pain in the right upper quadrant radiating to the right shoulder blade. There was no jaundice. X-ray examination at a hospital in another city was said to be negative. About six months before entry she had another attack of pain in the right upper quadrant associated with slight fever and jaundice that lasted for one month. The stools were clay colored, and the urine was positive for urobilinogen. X-ray examination showed the gall bladder to be poorly visualized. The patient was well again until seven weeks before entry, when she became jaundiced and the stools were clay colored. She had pruritus but no pain until the week of admission, when she began to have intermittent pain in the right upper quadrant accompanied by discomfort in the right flank and some pain in the right scapula. She was seen by her physician who found urobilinogen in the urine and a normal galactose-tolerance test.

The past history was negative except for a history of herpes zoster about two years before entry.

Physical examination showed a well-developed and well-nourished, jaundiced woman. The heart and lungs were normal. The abdomen showed no spasm, tenderness or masses. Murphy's sign was absent.

The blood pressure was 170 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a white-cell count of 13,400. The hemoglobin was 12 gm. per 100 cc. The urine was normal. The serum bilirubin was 12.1 mg. per 100 cc. direct, and 14.8 mg. indirect. The prothrombin time was 18 seconds (normal, 18 to 20 seconds).

The patient was given 4 mg. of hykinone twice a day intramuscularly and on the third hospital day an operation was performed.

*On leave of absence.

DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: The late Dr. E. P. Richardson was credited with saying that one could make a diagnosis of gallstones in three minutes or one could not make it at all. I think he was right. I do not know what the diagnosis was in this patient. There is not evidence enough on this record, and I presume that the patient did not present evidence enough to make it possible for me to make a diagnosis that I am happy with. I should have liked to have a little more information from the patient, just to clear up one or two things in my own mind. I should have wanted to know more about the attack of pain one and a half years before entry. How severe was that pain? Was it a definite and severe enough attack so that it would have meant gallstones to me?

DR. BENJAMIN CASTLEMAN: The opening sentence in the original record reads, "The patient out of a clear sky had an attack of pain in the right upper quadrant, with radiation into the right flank and in the region of the right shoulder blade."

DR. MCKITTRICK: But we want to know whether she had to bend over, whether the pain was extremely severe, whether she walked the floor—those are little points on which one makes a diagnosis. Was she perfectly well between the attack of a year ago and the one six months ago and until the onset of the jaundice seven weeks ago? I should like to be more clear in my mind about these things. The attack certainly in location and distribution is typical of biliary colic. The second attack, with fever and jaundice, was apparently consistent with a stone in the common duct, and the third attack was not at all typical. Therefore, I cannot make a diagnosis that satisfies me. I shall start with that premise and take the case up from another point of view and see what I can do.

The first thing is to try to decide whether this was an intrahepatic or an extrahepatic jaundice. In other words, did this woman have a hepatitis of some type or another or some extrahepatic pathology, such as gallstones, stricture of a duct or carcinoma in relation to the duct or the head of the pancreas? I cannot even make that differentiation clearly. There are certain things that suggest one thing, and some another. The urobilinogen does not mean much to me. I believe that urobilinogen is not found in the urine in a straight case of obstructive jaundice, except in the early stages, when there may still be bile in the intestinal tract that may be absorbed. It is likelier to be found in the urine in cases of liver damage. Is that correct, Dr. Beckman?

DR. WILLIAM BECKMAN: Yes.

DR. MCKITTRICK: The normal galactose-tolerance test offers some evidence against severe intrahepatic disease. The prothrombin time was normal. There is some suggestion that if the patient did have

hepatitis she did not have extensive liver destruction. Seven weeks of complete absence of bile from the stools, I presume, is a reasonable length of time for the average case of hepatitis to go on. It may not be too long, but is long enough so that one should begin to feel uneasy about it.

This woman had two attacks of pain that I should try to link up with the final diagnosis, but I must confess that at this moment I am not sure that I can do it in a logical manner. I am certain that the important decision to make is whether the patient had a surgical or a medical jaundice. Could one make a diagnosis of intrahepatic disease with sufficient accuracy to say that the patient should not have been operated on? That I cannot do. I believe that it was a surgical jaundice, not because I have strong conviction that it could not have been intrahepatic, but because she had two previous attacks of pain and for seven weeks had acholic stools. Having decided in my own mind that the patient should have been operated on, I should try to clarify in my mind — and the family also would have liked to know — what I thought that I was operating for, whether for gallstones or a carcinoma of the duct or the head of the pancreas.

This patient had had two previous attacks of pain. When a patient has had two such attacks, it seems to me that the question of gallstones cannot be excluded; no matter what the rest of the picture indicates. This patient did not present the classic picture of carcinomatous obstruction to the common duct, that is, the triad on which I place a great deal of importance — progressive and painless jaundice and a palpable gall bladder. The jaundice had progressed for seven weeks, and there was no pain at the onset of the jaundice, but the gall bladder was not palpable.

What about gallstones? Could gallstones give an attack of jaundice without pain? Of course they can. The mere fact that she had had two previous attacks of pain, one of which was associated with jaundice, is considerable evidence in support of the possibility that gallstones were present. On the other hand I think I am correct in saying that we do not see many women forty-nine years of age with a gallstone history dating back only one and a half years, during which time they have had only two attacks, in whom an attack due to a common-duct stone is initiated with painless jaundice. The biliary setup that usually gives painless jaundice is the contracted gall bladder where the stone has been squeezed down into the common duct and has settled down in the ampulla. This particular setup generally occurs in cases with long-standing biliary-tract disease and is infrequent.

It seems to me that we are left trying to put together from this bit of confusing evidence a reasonable diagnosis. I believe, although I have no strong conviction about it, that this jaundice was of extrahepatic origin. I must make a diagnosis of gall-

stones, although I am not happy about it. If I had talked with this patient, I believe that I should have found out something about these attacks of pain that would have clarified them in my mind. All I have to go on is the location, the sudden onset and the radiation. In the presence of a story of this sort I must make a diagnosis of gallstones.

Then the question comes up, If gallstones were present, were they the cause of the most recent attack? The mere fact that she had gallstones does not mean that she was being operated on for a condition secondary to the presence of such stones. Six months is a long time to go between attacks due to a stone in the common duct. Usually the attacks become more and more frequent as the stone gets into the common duct.

I could talk the rest of the day and not be any nearer to a definite diagnosis. I had better stop. I think, without conviction, that this was an extrahepatic condition. I will make a diagnosis of gallstones but I am not sure whether the obstruction to the cause of the jaundice, was a stone in the common duct or carcinoma related to the ductal system or possibly to the head of the pancreas. So long as one has to put one diagnosis in front of the other and rather than make two diagnoses, I will say that I favor a diagnosis of gallstones, with a stone impacted in the ampulla.

DR. MAURICE FREMONT-SMITH: The fact that she had one episode of jaundice and clay-colored stools, without pain, is additional argument for a stone, is it not?

DR. MCKITTRICK: It is a good logical course of events, but on the other hand, it is so good that I am suspicious. I am a little upset by the long interval — six months — between the second attack of pain and the development of painless jaundice.

DR. LLOYD MILLS: Regarding painless, progressive jaundice, a recent statistical survey of carcinoma of the head of the pancreas indicates that over 50 per cent of the patients had pain at some time during the course of the disease and that a smaller percentage had intermittent rather than progressive jaundice.

DR. MCKITTRICK: I shall answer that in a different way. Whenever there are variations, one has to be careful of conclusions. When one has a patient, however, who says that the family noticed that her eyes were yellow and she becomes more and more jaundiced, that jaundice was not initiated with an attack of pain — in other words, the jaundice was painless. If these two things happen and one can palpate a large smooth gall bladder, they nearly always mean a malignant obstruction to the common bile duct.

CLINICAL DIAGNOSES

Chronic cholecystitis.
Cholelithiasis?

DR. MCKITTRICK'S DIAGNOSES

CASE 30382

Cholelithiasis.
 Choledocholithiasis?
 Carcinoma of common bile duct or head of pancreas?

ANATOMICAL DIAGNOSES

Adenocarcinoma of right hepatic duct, with extension into the entire common duct.
 Cholelithiasis.
 Chronic cholecystitis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At operation the surgeon removed a thickened distended gall bladder; the right and left hepatic ducts and the common duct were markedly distended, being two or three times the normal diameter. After the cystic duct was clamped and compressed in such a manner as to force its contents into the common duct, the common duct was opened and a cast of the duct composed of greenish-black, rubbery, tissue-like material was pulled from the entire common duct. Similar material was suctioned from both hepatic ducts. I was called to the operating room and shown this material. The outside was coal black, but the inside was a mottled pinkish red and looked like definite tissue. A frozen section proved it to be an adenocarcinoma. The surgeon was able to scoop out this material easily because it was not adherent. The origin of the tumor was believed to be in the right hepatic duct, because its wall was thicker and rougher than the rest of the duct. There were no definite stones in the common duct, but the gall bladder had small blackish stones. I suppose that stones had been passing through the common duct for some time. A T-tube was placed in the common duct.

DR. MCKITTRICK: Was the ampulla patent?

DR. CASTLEMAN: Yes.

DR. LAURENCE L. ROBBINS: A postoperative cholangiogram shows a constant defect in the right hepatic duct.

DR. MCKITTRICK: That makes a perfectly good story. She could have had a hemorrhage from the tumor, and the blood could have passed down and caused an attack of pain the same as that of gallstones. The only reason that one says gallstones is that there is not much else in the biliary tree, except gallstones, to give attacks of pain. The last attack of jaundice can be explained by the propagation of this tumor mass down the common duct and gradual occlusion in that way.

DR. CASTLEMAN: Do you think anything more can be done surgically?

DR. MCKITTRICK: No; it is a difficult area to approach.

PRESENTATION OF CASE

A forty-seven-year-old married woman was admitted to the hospital in semicoma.

Because of the patient's stuporous state only a meager history was obtainable from relatives and her private physician. About five months prior to admission she first noted some rectal bleeding, which continued intermittently. The amount and color of the blood could not be ascertained. About six weeks before entry she developed lower abdominal pain, which became progressively severer and was associated with increasing constipation. For about four days prior to entry she was unable to move her bowels although she had a frequent and intense desire to do so. A physician was called and prescribed 0.02 gm. of pantopon every four hours. This regimen was followed religiously except when the patient slept. During the twenty-four hours before admission she became stuporous and ceased to void and during that time she received only 0.02 gm. of pantopon.

The patient had gonorrhea twenty years prior to admission and was treated for a year. About a year later she had an attack of redness and swelling of the knees and the joints of the feet, which cleared up after bed rest. Twelve years before entry she had attacks of vomiting and pain in the right upper quadrant, following which a cholecystectomy, choledochostomy and routine appendectomy were performed, with relief of symptoms. A few small stones were found in the gall bladder and one was removed from the common duct. At that time several urine examinations revealed a specific gravity ranging from 1.018 to 1.032, with no albumin and a sediment containing numerous white cells, occasional red cells and a rare cellular cast. For about ten years before admission she had had nocturia two to four times.

Physical examination revealed an obese woman in semicoma, breathing stertorously. She responded to shaking but not to painful stimuli. The pupils were very small, round, regular and equal, and there was only slight reaction to light. The mouth and tongue were dry. There was a uriferous odor to the breath, and a uremic frost was noted. The lungs were clear, and the heart, except for a rapid rate, was negative. The abdomen was moderately distended and there was slight tenderness to deep palpation in the lower portion. The deep tendon reflexes were active and equal, the abdominal reflexes were absent, and the Hoffmann and Babinski signs were positive. Pelvic examination revealed a prolapsed and lacerated cervix, but no masses could be felt in the vaults. Digital examination revealed a firm, rather smooth, fixed mass on the anterior wall of the rectum about 8 cm. above the anus; a small

amount of bright-red blood stained the examining finger.

The temperature was 98.6°F., the pulse 100, and the respirations 18. The blood pressure was 120 systolic, 75 diastolic.

Examination of the blood revealed a red-cell count of 4,000,000, with 70 per cent hemoglobin, and a white-cell count of 24,400, with 86 per cent neutrophils. A catheterized urine specimen had a specific gravity of 1.010, with an acid reaction, a +++ test for albumin and 10 white cells per high-power field; no sugar or acetone was present. The blood nonprotein nitrogen was 130 mg. per 100 cc., the serum protein 6 gm., and the chloride 89 milliequiv. per liter. A Hinton test was negative. Roentgenographic examination of the abdomen was unsatisfactory; it revealed considerable gas in the cecum and sigmoid, but no definite dilated loops of small bowel could be seen. An electrocardiogram was within normal limits. A biopsy of the rectal mass revealed adenocarcinoma.

Following admission the patient was catheterized and a considerable amount of pale urine was obtained. A lumbar puncture revealed clear fluid with normal dynamics. The respirations fell to 10 per minute, and she was treated with picrotoxin, receiving 14 mg. over a period of six hours, followed by inhalation of carbon dioxide. There was temporary improvement for several hours, but the respirations soon fell to their former level. On the third hospital day the ureters were catheterized. The catheters were passed with ease but no urine was obtained. Fluids were administered intravenously up to 2500 cc. daily, principally dextrose in water and some sodium lactate. By the fifth hospital day she had begun to void, her sensorium became clearer and her respirations had increased to 16 to 20 per minute. The ureteral catheters were then removed.

In spite of a fair urine output and apparent improvement enabling the patient to sit out of bed for short periods, the nonprotein nitrogen continued to rise, eventually reaching 235 mg. per 100 cc. The blood carbon dioxide content was 17.5 milliequiv. per liter. The blood pressure on several occasions reached 190 systolic, 110 diastolic, although it was usually lower. On the eighth hospital day a difference in the circumference of the two legs was noted. Homans's sign was negative. A prophylactic superficial ligation of a leg vein was done. On the following day the urine was red and cloudy, with a specific gravity of 1.010, an alkaline reaction, a +++ test for albumin and a sediment containing innumerable red cells and many white cells but no casts.

The patient's condition rapidly became worse. On the fourteenth hospital day she again became anuric and 25 per cent glucose and plasma were administered intravenously in a vain attempt to induce diuresis. The blood pressure fell to 120 systolic, 60 diastolic, and she vomited frequently. Gastric

lavage produced 750 cc. of bloody fluid, and she placed on constant gastric suction. She died on fifteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: In this case we are presented with a pathological diagnosis of adenocarcinoma apparently of rectal origin. This accounts well for the rectal bleeding and for the progressive constipation and abdominal pain. For the rest, it is necessary to establish the cause of the patient's anuria and death.

The first thought that naturally arises is that the terminal picture might have been due to extension of the malignant tumor. It is an interesting fact, however, that death by renal failure is a very common complication of cancer of the lower bowel, in contrast to cancer of the cervix and of the urinary tract itself. Metastasis from rectal carcinoma characteristically goes to lymph nodes and to the liver, the portal venous system, and spares the urogenital tract. We have no evidence to suggest that the pelvic tumor was large enough to compress the ureters, and finally, it is stated that catheters could be passed easily through both ureters. We are forced to conclude that the urinary suppression was of renal or prerenal origin.

What evidence do we have regarding the possibility that the patient had chronic renal disease? Twelve years before entry, at the time of the bladder operation, several urine examinations showed abnormal sedimentary findings, including red cells but no albumin. Also, for ten years before admission she had had nocturia. Unfortunately, we do not have a record of her blood pressure at any time prior to admission in coma, nor is there any examination of the eye grounds recorded. Either of these might have given us information whether this episode occurred in the course of chronic nephritis. Without them, we can only say that the history is suggestive of chronic renal disease which might or might not have been severe.

Assuming that the patient had indeed suffered from chronic glomerulonephritis or from chronic vascular disease with emphasis on renal impairment, what precipitated the present acute and fatal episode? Two possibilities stand out. This may, in the first place, have been an acute exacerbation of an acute hemorrhagic nephritis punctuating the course of chronic nephritis. It is perfectly possible, although not frequent, for acute nephritis to manifest itself by acute complete urinary suppression. In such a case the blood pressure would at first be normal, in the absence of chronic nephritis with hypertension, but this denies the first postulate, and we should have to minimize the chronic nephritis in favor of acute nephritis *de novo*. Moreover, when urinary flow was obtained, the urine was at first clear. The hypothesis of acute nephritis with

without a previous renal background is not wholly satisfactory.

It seems to me that the case of a patient who is admitted in coma following dosage with pantopon, shows signs of morphine toxicity, and who at the same time develops fatal anuria, ought if possible to be explained on the basis of the drug. Sufficient doses of morphine depress blood pressure, and secondarily cause decrease or disappearance of urinary flow. The patient, however, had a normal blood pressure on admission. It is possible that she may have previously suffered from marked hypertension, although the clinical examination of the heart and the electrocardiogram do not suggest this, and that secretion of urine ceased when the blood pressure was brought down to a normal level, just as it may when the blood pressure of a normal person goes to shock levels. The second episode following vein ligation, on the other hand, being ushered in by hematuria without casts, suggests acute renal disease of some sort. Perhaps the previous ureteral instrumentation was responsible for the gross hematuria.

If this patient had received an earlier course of sulfonamide therapy, with dosage again just before admission, and perhaps again at the time of vein ligation, it would seem to me that this was a clear case of renal shutdown on a sulfonamide-sensitivity basis, and that we might expect to find inflammatory and granulomatous interstitial lesions in the kidneys. If she did get sulfonamides, however, this has been forgotten. Other drugs have occasionally been mentioned as factors causing anuria, and sensitization to opium derivatives, as evidenced by skin eruptions, does occur. Morphine has not to my knowledge been implicated in a picture such as this. We have nothing else in this case to suggest sensitization, such as skin rash, eosinophilia or fever. We do not even know for certain that morphine was given at the time of the vein ligation, although it probably was, the procedure being done under local anesthesia. The sequence of events and the lack of an entirely satisfactory diagnosis, however, tempt one to entertain such a thought.

Other causes of anuria, such as massive renal infarction, seem to have little to offer in this case. Extensive liver metastasis from rectal carcinoma might cause hepatic failure, with a high nonprotein nitrogen because of elevated amino nitrogen, and might interfere with the detoxication of morphine. I do not gather from the history that such unusually massive hepatic metastasis occurred, and we should still have to explain the anuria.

CLINICAL DIAGNOSES

Carcinoma of rectum.

Renal insufficiency, with uremia and anuria.

DR. BRUES'S DIAGNOSES

Adenocarcinoma of rectum.

Chronic and acute glomerulonephritis?

Acute interstitial renal disease, sensitization type?

ANATOMICAL DIAGNOSES

Acute pyelonephritis, with multiple small abscesses.

Chronic vascular nephritis.

Cardiac hypertrophy, hypertensive type, moderate.

(Uremia.)

Cystitis, acute and chronic.

Adenocarcinoma of rectum, with metastases to liver.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The rectal carcinoma was located just below the rectosigmoid junction, and several small metastatic nodules were present in the liver. As Dr. Brues predicted, there were no metastases in the region of the ureters and no ureteral obstruction was apparent.

The kidneys together weighed 200 gm., the right a little heavier than the left. The capsules were thickened and adherent. The parenchyma was fairly soft, and the cortical and medullary markings were difficult to visualize. The cortex was somewhat narrowed and several yellowish-brown pin-point areas were present. Microscopically there was evidence of old vascular disease, especially of the arterioles, with hyalinization of a relatively small number of glomeruli. The remaining glomeruli appeared normal, and there was very little tubular atrophy or tubules filled with colloid casts, which should rule out chronic glomerulonephritis and chronic pyelonephritis, respectively, as the cause of the underlying renal disease. Superimposed on the chronic vascular nephritis was an acute pyelonephritis characterized by multiple small abscesses filled with bacteria, by pus in the tubules and by a fairly extensive polymorphonuclear infiltration of the parenchyma. The ureters were not dilated or thickened. The bladder was moderately inflamed.

The cause of the acute pyelonephritis is not easy to explain. So far as we know, the patient had not received any of the sulfonamides, and the purulent rather than granulomatous character of the inflammation is rather against a sensitivity reaction. Although the bladder was moderately inflamed, I believe that the infection was hematogenous rather than ascending from the lower urinary tract.

The heart weighed 410 gm. and showed left ventricular hypertrophy.

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

THREE SCORE AND TEN

THE longevity of the American people, the statisticians of the Metropolitan Life Insurance Company* tell us, reached its all-time peak in 1942. In that year white girl babies reaching their first birthday had, on an average, seventy years of life ahead of them, exceeding by one year the biblically allotted three score and ten. Not until their fortieth birthday did white males achieve an average expectancy of thirty additional years, thus suggesting, although by no means proving, that Methuselah was a lady.

*Statistical Bulletin. Metropolitan Life Insurance Company. Vol. 25, April, 1944. No. 4.

Actually, the figures of 1942 give us striking evidence of what improved living conditions have done for the race, since in that year the average length of life of all our people, white and colored, was practically sixty-five years, a gain of nearly sixteen years since 1900, when the average length of life was forty-nine years. The slow rise over earlier recorded expectations of life is, of course, a hundred-fold and more.

The ladies have always been better insurance risks than have the gentlemen, even in the lush years of peace and plenty. Since the turn of the century, for instance, the distaff side of the family has been granted an average increase in length of life of over seventeen years, as compared with the fifteen years accorded to the sterner sex; and even at the age of forty the remaining years for females have increased nearly five years, as compared with the miserly two and a half years increase allotted to the breadwinners of the families.

Among our colored population a noticeable improvement in life expectancy has also taken place, with an increase of nearly twenty-two years for males, and twenty-three years for females. But this substantial advance only brings the colored population up to a 1942 life expectancy of fifty-four years for males, and fifty-eight years for females — about the expectancy that the white population of this country had already achieved some twenty years earlier.

These figures, even as we realize that they are brought about largely by reductions in infant mortality and in the mortality of childhood, put a different and a more benign emphasis on the possibilities of a pleasant old age. The average person of sixty-five, for example, now faces the prospect of thirteen more or less pleasant years ahead and may even reach the age of eighty or more, if his health is above the average.

Some falling off in this expectation has taken place in 1943 and will continue in 1944 — years of stress and strain and overwork, and moreover years in which a minor epidemic of respiratory infections exacted an increased toll of lives. The future, however, if we consolidate our gains, holds out an increasingly pleasing prospect.

PNEUMONIA IN SHIPBUILDERS

THE recent tremendous addition to the number of welders engaged in essential war industries has brought into focus the possibility of an increase in respiratory diseases in such workers resulting from the character of their tasks. Symptoms of various sorts are attributed by these workers and by many physicians to the fumes to which they are exposed. The symptoms may simulate those of acute systemic or respiratory infections or those of chronic respiratory diseases. The former are encountered most frequently during the season when acute respiratory infections have the greatest incidence, which suggests an increased susceptibility of such workers to the prevalent infections. The latter are usually recognized in x-ray films of the chest taken routinely or because of respiratory symptoms.

With respect to the lung changes in electric-arc welders, Sander¹ has recently pointed out the importance of preventive measures for the protection of workers. He finds that electric-arc welding that is done in large rooms, or where the fumes are not allowed to concentrate excessively near the breathing level, does not cause lung changes even after many years of work. On the other hand, excessive inhalation of concentrated fumes, especially in confined and unventilated spaces, may cause siderosis. The siderosis so produced consists of the deposit of inert iron pigment in the lymphatics without fibrous-tissue proliferation and without progressive changes after the exposure is materially decreased. Sander also states that welding and siderosis do not predispose to tuberculosis or to other lung infections, nor do they cause functional impairment of the lungs or symptoms referable to the lungs. Acute irritations of the throat, however, may occur with too prolonged work in dense clouds of fumes, but these appear to be transitory and to leave no residual. He believes that any respiratory involvement may be prevented in welding, even with the most prolonged and confined work, if proper precautions are taken by installing adequate exhaust ventilation and by using ventilated helmets or positive-pressure respirators.

Another study, carried out by physicians of the Permanente Foundation Hospital² among the workers of the Kaiser Richmond Shipyards on the West

Coast, suggests that acute pulmonary infections are neither more frequent nor more serious among shipbuilders than among similar persons in other walks of life. This study covered a twelve-month period during which 864 patients with pneumonia were treated. Some of the findings and the conclusions based on this study are worth mentioning.

The annual frequency rate of pneumonia at the shipyards was 9.5 per 1000 workers. This is probably a high incidence, but, as the authors point out, there are no reliable data to indicate that it is any different in shipyard workers than among the general population. It certainly is lower than the rate among certain types of workers in the iron and steel industries, but it is higher than the average incidence reported for all iron and steel workers.³

The type of pneumonia among the shipyard workers was in no way different from that among the general population. There was no indication that workers who had recently migrated to the region of the shipyards from other states were more susceptible to pneumonia than those who had lived in that region for a long time. The incidence rate for pneumonia was independent of the length of employment at the yards, as well as of the type of work done by the workers. In particular, pneumonia was no more frequent among welders than among those doing other jobs, such as laborers, electricians and machinists.

The gross mortality for the entire group of patients with pneumonia was 8.2 per cent. This figure, as the authors point out, compares favorably with that achieved in many of the best clinics throughout the country. A large proportion of the patients were over forty years of age and had more than one lobe involved. The mortality in patients under forty years of age was less than 4 per cent, and in those having only a single lobe involved it was less than 5 per cent. These low fatality rates suggest that the conditions to which the shipyard workers were exposed did not aggravate the prognosis in those who acquired pneumonia. More likely, however, it reflects the fine type of medical care that these patients received.⁴

Apparently the United States Maritime Commission has been deeply concerned about the widespread rumors among workers and physicians that

welding causes respiratory disease. The commission is, therefore, anxious to give the findings among the Kaiser shipyard workers widespread publicity in order not to discourage people interested in this form of employment.

REFERENCES

1. Sander, O. A. Further observations on lung changes in electric arc welders. *J. Indust. Hyg. & Toxicol.* 26:79-85, 1944.
2. Collen, M. F., Dybdahl, G. L., and O'Brien, G. F. Study of pneumonia in shipbuilding industry: epidemiology and management of 864 cases over a one-year period in Kaiser Richmond Shipyards. *J. Indust. Hyg. & Toxicol.* 26:1-7, 1944.
3. Brundage, D. K., et al. Frequency of pneumonia among iron and steel workers. *Pub. Health Bull.* No. 202. 51 pp. Washington, D. C.: Government Printing Office, 1932.
4. Collen, M. F., and Dybdahl, G. L. Management of pneumonia: review of 517 cases. *Permanente Found. M. Bull.* 1:14-24, 1943.

MASSACHUSETTS MEDICAL SOCIETY

STATED MEETING OF THE COUNCIL

A stated meeting of the Council of the Massachusetts Medical Society will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 4, 1944, at 10:00 a.m.

Business:

1. Call to order at 10:00 a.m.
2. Presentation of record of meeting held May 22, 1944. (Published in the *New England Journal of Medicine*, issue of July 27, 1944.)
3. Reports of standing and special committees.
4. Appointment of an auditing committee.
5. Fill any vacancies in the offices of the Society.
6. Such other business as may lawfully come before this meeting.

MICHAEL A. TIGHE, M.D., Secretary

DEATH

CRAWFORD — Francis X. Crawford, M.D., of Dorchester, died August 19. He was in his seventy-second year.

Dr. Crawford received his degree from Harvard Medical School in 1898. He was a member of the staffs of St. Elizabeth's and the Carney hospitals and a member of the American Medical Association.

His widow and four sisters survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

REIMMUNIZATION AGAINST TYPHOID FEVER

When a working basis for typhoid vaccination was established thirty-five years ago in the United States Army by Brigadier General (then Captain) F. F. Russell, the necessity for periodic reimmunization was recognized. At that time the policy of repeating the complete course of three doses of vaccine at three-year intervals was established. In recent years, the vaccination procedure as a whole has been extensively reinvestigated by the Typhoid Research Unit at the Army Medical Center. This group has found that adequate reimmunization can be obtained with a single dose instead of three doses of vaccine.

It is now well established that this single reimmunizing dose may be administered in one of two ways — 0.5 cc. subcutaneously or 0.1 cc. intradermally. Furthermore, it appears that this single dose is effective regardless of the interval since the last complete course of immunization.

The use of a single dose greatly simplifies the reimmunization process and also markedly reduces the incidence of local and systemic reactions, which are much more frequent and severe after reimmunization than during a first immunizing course.

The official recommendations are as follows:

- (1) The administration of full courses of typhoid vaccine to persons who have previously been immunized against typhoid fever is unnecessary and should be abandoned.
- (2) Wherever renewal of immunity is indicated in a previously vaccinated person, a single dose of vaccine should be administered.
- (3) This dose should consist of 0.5 cc. subcutaneously or 0.1 cc. intradermally. Although there is evidence that intradermal injections are somewhat more effective than those given subcutaneously, it should be noted that the smaller dose is probably ineffective if it happens to be given subcutaneously instead of intradermally.
- (4) The ideal interval between successive typhoid immunizations is one year, but a lapse of time greater than this between successive immunizations does not necessitate the administration of a full three-dose course of inoculations.
- (5) Whenever there is doubt concerning the best immunization procedure to follow, it is suggested that the physician in charge consult one of the persons given below regarding the performance of a protection test on the patient's serum. This test, which can be done in four or five days at the Antitoxin and Vaccine Laboratory, is considered the best available method of determining a patient's immunity status.

The Director, Division of Biologic Laboratories
375 South Street, Jamaica Plain
(Telephone, ARNold 4127)

The Director, Division of Communicable Diseases
State House, Boston
(Telephone, CAPitol 4600)

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1944

DISEASES	RÉSUMÉ		
	JULY 1944	JULY 1943	SEVEN-YEAR MEDIAN
Anterior poliomyelitis.	23	1	4
Chancroid	1	*	*
Chicken pox	637	400	402
Diphtheria	14	6	9
Dog bite	1076	1115	1193
Dysentery, bacillary	23	2	11
German measles	60	468	30
Gonorrhea	356	355	355
Granuloma inguinale	3	*	*
Lymphogranuloma venereum	66	12	1
Malaria	876	1468	1159
Measles	32	51	5
Meningitis, meningococcal	1	3	1
Meningitis, Pfeiffer-bacillus	2	5	1
Meningitis, pneumococcal	—	—	1
Meningitis, staphylococcal	4	—	1
Meningitis, streptococcal	1	—	1
Meningitis, other forms	1	9	1
Meningitis, undetermined	434	244	358
Mumps	86	93	147
Pneumonia, lobar	11	19	9
Salmonella infections	246	439	261
Scarlet fever	303	363	407
Syphilis	235	191	288
Tuberculosis, pulmonary	19	6	23
Tuberculosis, other forms	2	7	4
Typhoid fever	284	317	521
Undulant fever	—	—	—
Whooping cough	—	—	—

*Made reportable December, 1943.

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENT

Anterior poliomyelitis, although showing a definite increase over the same period in 1943, does not indicate that epidemic proportions may be reached. It is impossible at this time to determine what the trend will be in the months ahead.

Mumps has shown an increase of almost 50 per cent over the corresponding period last year.

Dysentery has shown the usual seasonal increase.

Malaria has shown an increase, but the increase is primarily due to the return of service men from foreign fields.

The usual seasonal decline is noted in several of the diseases.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from: Burlington, 1; total, 1.
Anterior poliomyelitis was reported from: Ayer, 1; Boston, 2; Camp Myles Standish, 1; East Longmeadow, 1; Hinsdale, 1; North Adams, 1; Pittsfield, 3; Quincy, 1; Springfield, 5; West Springfield, 6; Winchester, 1; total, 23.

Diphtheria was reported from: Boston, 4; Brookline, 1; Cambridge, 1; Lawrence, 1; Methuen, 3; New Bedford, 1; Revere, 1; Somerville, 1; Taunton, 1; total, 14.

Dysentery, bacillary, was reported from: Worcester, 11; Wrentham, 12; total, 23.

Hookworm disease was reported from: Framingham, 1; total, 1.

Malaria was reported from: Ashland, 1; Cambridge, 1; Camp Edwards, 11; Cushing General Hospital, 22; Fort Devens, 20; Gloucester, 1; Hanson, 1; Lynn, 1; Medford, 1; Milford, 1; Quincy, 1; Reading, 1; Somerville, 1; Springfield, 1; Waltham, 1; Winchester, 1; total, 66.

Meningitis, meningococcal, was reported from: Boston, 6; Braintree, 1; Chelsea, 1; Everett, 1; Fairhaven, 1; Grafton, 1; Haverhill, 1; Lowell, 2; Lynnfield, 1; Malden, 1; Melrose, 1; Methuen, 1; New Bedford, 1; Newton, 1; Pittsfield, 2; Quincy, 1; Revere, 1; Salem, 1; Saugus, 1; Shrewsbury, 1; Spencer, 1; Springfield, 2; Webster, 1; Worcester, 1; total, 32.

Meningitis, Pfeiffer-bacillus, was reported from: Tisbury, 1; total, 1.

Meningitis, pneumococcal, was reported from: Boston, 1; Dartmouth, 1; total, 2.

Meningitis, streptococcal, was reported from: Adams, 1; Barnstable, 1; Orleans, 1; Springfield, 1; total, 4.

Meningitis, other forms, was reported from: Cambridge, 1; total, 1.

Meningitis, undetermined, was reported from: Millbury, 1; total, 1.

Salmonella infections were reported from: Cambridge, 1; Dedham, 1; Lawrence, 1; Malden, 1; Methuen, 1; Salem, 2; Somerville, 1; Waltham, 1; Worcester, 2; total, 11.

Septic sore throat was reported from: Boston, 3; North Adams, 1; Quincy, 1; total, 5.

Tetanus was reported from: Springfield, 1; total, 1.

Trichinosis was reported from: Marblehead, 1; Norwood, 1; total, 2.

Typhoid fever was reported from: Boston, 1; Fall River, 1; total, 2.

Typhus fever was reported from: Boston, 1; total, 1.

Undulant fever was reported from: Boston, 1; Hatfield, 1; Middleboro, 1; total, 3.

CORRESPONDENCE

INVENTORY OF DEMEROL

To the Editor: A form letter has recently been sent to all narcotic registrants relative to the substance isonipicaine, commonly known as "Demerol," which by a recent act of Congress has been brought under the provisions of the federal narcotic laws.

All registrants were called on to file an inventory with the Collector, not later than September 1, of Demerol on hand as of July 1. Many are under the impression that no inventory was required if they had no Demerol to report. This is not correct. In cases where registrants have no Demerol on hand, their inventory should so state. Those who failed to file on the required date should do so immediately.

The original sworn copy is to be sent in to the Collector, and the duplicate retained.

DENIS W. DELANEY, *Collector*

Internal Revenue Service
Office of the Collector
Boston 9

CO-EXISTENCE OF GALLSTONES AND ULCER

To the Editor: In discussing one of the case records of the Massachusetts General Hospital (Case 30262) in the June 29 issue of the *Journal*, Dr. Wyman Richardson made the following statement: "The combination of gallstones and ulcer in the same patient is almost unheard of. . . . It is a striking thing that the ulcer habitus and the gallstone habitus are quite different, and I do not believe that I have ever seen the two diseases in the same patient." Since these cases are widely read, frequently quoted and generally considered authoritative, I believe the above quotation should be challenged.

Many years ago the Drs. Mayo emphasized an abdominal triad — appendicitis, gall-bladder disease and ulcer — in the same patient.

In 1931, Dr. Franklin W. White and I (*New Eng. J. Med.* 205:793-797, 1931) reported a case of gastric ulcer and gallstones. Therein we stated, "The presence of gallstones naturally does not exclude ulcer; both may be present, in fact the association of lesions in the duodenum or stomach and the gall bladder is not at all rare." I am still subscribing to this view on the basis of my own experience and that of many others.

In 1943, Dr. S. A. Robins and I (*Am. J. Digest Dis. & Nutrition* 10:445-447, 1943) quoted 3 patients who had had subtotal gastrectomy for intractable ulcers and later developed gallstones. I can also recall at least 2 patients who were operated for gallstones and showed at the accompanying exploration of the abdomen an active ulcer in the duodenum.

The day after I read the discussion of the above case I saw a patient who gave a twenty-year history of an ulcer. A duodenal ulcer was demonstrated by x-ray study in 1938 and again in 1944, and at the latter examination two large gallstones were also shown.

I have seen both in private and in hospital practice other cases in which a peptic ulcer and gall-bladder disease were present in the same patient. I have no records on hand to substantiate these cases, but I do not believe that it is necessary in view of the above facts.

I. R. JANKELSON, M.D.

485 Beacon Street
Boston 15

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Medical Parasitology: A laboratory manual. By Jacques Yetwin, M.S., M.D., medical technologist and associate professor of parasitology, Middlesex University School of Medicine, Waltham, Massachusetts. Fourth edition. 8°, cloth, 126 pp., with 127 illustrations. Boston: Boston Linotype Print, Incorporated, 1944. \$3.00.

This manual of a laboratory course has been modified to suit existing conditions brought on by the present war. The time allotted to the course has been increased from sixty to seventy-five hours. Mycology, as a rule, has been omitted, since it is taught in the course on bacteriology. The illustrations have been taken from a collection of five hundred slides of important parasites.

Baby Doctor. By Isaac A. Abt, M.D. 8°, cloth, 310 pp. New York: Whittlesey House, 1944. \$2.50.

This autobiography of an eminent pediatrician who has practiced his specialty for fifty years naturally reflects the history and advances in pediatrics during that period.

Health and Hygiene: A comprehensive study of disease prevention and health promotion. By Lloyd Ackerman, Ph.D., Western Reserve University. 8°, cloth, 895 pp., with 59 illustrations and 27 tables. Lancaster, Pennsylvania: The Jaques Cattell Press, 1943. \$5.00.

This popular treatise on health is based on the latest information and includes thorough discussions of nutrition, sex, infection, inflammation, immunology, mental attitudes and behavior problems. The first three parts are historical. The work is well written and printed with a good type on good paper.

The Hospital in Modern Society. Edited by Arthur C. Bachmeyer, M.D., director, University of Chicago Clinics, and director, Hospital Administration Course, University of Chicago; and Gerhard Hartman, Ph.D., director, Newton Hospital, Newton Lower Falls, Massachusetts. 8°, cloth, 766 pp., with 3 illustrations and 5 tables. New York: The Commonwealth Fund, 1943. \$5.00.

In this compact volume will be found a collection of readings selected from the literature in the hospital field and in the allied fields of medicine, public health, management and organization, law, sociology and psychology, comprising the essence of the published material on hospital administration. The work is intended for individuals interested in all aspects of hospital administration, and although not exhaustive, it represents an endeavor to assemble material that is so widely dispersed in the literature that it is unavailable to the average reader.

Gastro-Enterology (in three volumes). By Henry L. Bockus, M.D., professor of gastroenterology, University of Pennsylvania Graduate School of Medicine; and colleagues at the University of Pennsylvania Graduate School of Medicine. Volume II. *The Small and Large Intestine and Peritoneum: Diagnosis and treatment of disorders of the small intestine, colon, peritoneum, mesentery and omentum.* 4°, cloth, 975 pp., with 311 illustrations and 53 tables. Philadelphia and London: W. B. Saunders Company, 1944. \$12.00.

This second volume of a complete treatise of the gastrointestinal tract has been published on time despite the great difficulty encountered during the present war. It is hoped that the third volume on the liver, biliary tract and pancreas may be published as promptly.

NOTICES

SUFFOLK CENSORS' MEETING

The censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, Boston, on Thursday, December 7, at 4:00 p.m.

FELLOWSHIPS IN CHILD PSYCHIATRY

A limited number of fellowships are being offered for training in extramural child psychiatry. Selection for these fellowships is made by the National Committee for Mental Hygiene following the recommendation of eligible applicants for appointment. These fellows will spend one or two years in a selected clinic, the term and plan of the fellowship to be determined by the peculiar needs of the applicant. The training is pursued according to a definite plan related to the probable future functions of these fellows. Candidates for fellowship award should have had at least a general internship and two years devoted to psychiatry in an approved mental-hospital service, in addition to other qualities fitting them for extramural service. Since this provision of training fellowships comes in response to a definite paucity of personnel in this field, peculiarities of the demand are considered in making appointments. The stipends vary slightly with location and status of the fellow but in general range between \$2000 and \$2400.

Requests for further information about these fellowships, and applications therefor, should be addressed to Dr. Milton E. Kirkpatrick, National Committee for Mental Hygiene, 1790 Broadway, New York 19, New York.

PUBLIC HEALTH CONFERENCE

The Second Wartime Public Health Conference will be held in the Hotel Pennsylvania, New York City, on October 2, 3, 4 and 5.

Thirteen organizations will co-ordinate their own conferences, demonstrations and symposiums with the seventy-third annual business meeting of the American Public Health Association in discussion and evaluation of all phases of public-health protection that will have far-reaching effects in the postwar world.

New global frontiers in public health will be reported by some of the pioneers who helped establish them. New diseases encountered by American armed forces in various parts of the world, insect problems, control measures against importation of disease by returning veterans and new disinfectants are among the things that will be discussed.

From the civilian front will come reports on sanitary engineering, laboratory technic, milk control, dental care, social and industrial hygiene, school health, public-health nursing, wartime nutrition, wartime food and drug adulteration, air-borne infections and various other diseases.

More than three hundred health officials will read papers or participate in panel discussions. The organizations meeting jointly with the American Public Health Association are as follows: American Association of Public Health Dentists, American Film Center, American School Health Association, American Social Hygiene Association, Industrial Nursing Consultants, Municipal Public Health Engineers, Reciprocal Sanitary Milk Control, State and Provincial Public Health Laboratory Directors, State Directors of Public Health Education, State Directors of Public Health Nursing, State Sanitary Engineers, Teachers of Preventive Medicine and National Publicity Council for Health and Welfare Services.

AMERICAN BOARD OF INTERNAL MEDICINE

The next written examination of the American Board of Internal Medicine will be held on February 19, 1945. The closing date for the acceptance of applications is December 15, 1944.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 28

SATURDAY, SEPTEMBER 30

*10.00-11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, OCTOBER 2

*12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 3

*12:15-1:15 p.m. Clinicoröntgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, OCTOBER 4

Medicolegal conference, Mallory Institute of Pathology, Boston.

*12.00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

OCTOBER 3-5. Second Wartime Public Health Conference. Notice elsewhere on this page.

OCTOBER 2-7. Seminar in Legal Medicine, Harvard Medical School. Page 110, issue of July 20.

OCTOBER 3-5. American Public Health Association. Page ix, issue of March 30.

OCTOBER 9-20 1944 Graduate Fortnight of the New York Academy of Medicine. Page xvii, issue of July 27.

OCTOBER 10. New England Society of Anesthesiology. Page xvii, issue of September 7.

OCTOBER 13. Mental Conditions Resulting from the War. Dr. C. A. Bonner. Pentucket Association of Physicians. 8:30 p.m., Haverhill.

OCTOBER 16-November 3. Third Postgraduate Course in Industrial Medicine. Page six, issue of September 14.

(Notices continued on page xv)

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ABNORMAL CARBOHYDRATE METABOLISM IN HUMAN THERMAL BURNS*

Preliminary Observations

F. H. L. TAYLOR, PH.D.,† STANLEY M. LEVENSON, M.D.,‡ AND MARGARET A. ADAMS, A.B.§

BOSTON

UNTIL the last few years shock has been apparently the major cause of death in the first few days following severe burns. It is now well established that it can be prevented or successfully treated in most patients if they are seen soon enough after thermal injury. There are, however, still many early deaths among severely burned patients, despite the fact that clinical shock has not existed at any time or, if present, has been corrected. A series of investigations on the biochemical and physiologic changes occurring after thermal burns are being carried out with the view of determining the significance and therapeutic implications of these changes. The present communication is concerned with the preliminary observations on changes in carbohydrate metabolism and, to a lesser extent, with changes in nitrogen metabolism. Electrolyte studies carried out on these patients will be reported later.

Hyperglycemia occurring soon after burns has been reported in human beings by Davidson,¹ Underhill et al.,² Martin³ and McIver.⁴ In general, the rise in blood sugar was proportional to the severity of the burn. Many patients with minor burns showed no hyperglycemic response. The blood-sugar level in most cases returned to normal in twenty-four to forty-eight hours.

Lundberg and Backman⁵ and Slocum and Lightbody,⁶ working with burned rabbits, and Lambrecht, Driessens and Waremboorg,⁷ working with burned dogs, found similar results. The rise in blood sugar occurred within an hour after injury. The height and duration of the hyperglycemia was proportional to the severity of the burn. Thus, Lundberg and

Backman report that in first-degree burns the blood sugar may increase to a level as high as 172 mg. per 100 cc. thirty minutes after the burn: at the end of two hours the level was again normal. Animals with second-degree burns showed rises of the blood-sugar level as high as 215 mg. and it returned to normal at the end of seven hours. With third-degree burns, the level rose to 326 mg. and at the end of twenty-four hours the blood sugar was still at an elevated level (154 mg.).

Greenwald and Eliasberg⁸ reported hypoglycemia in 2 patients studied for the first time two and five days, respectively, following the burn injury. From their studies on burned rabbits they suggest that an early hyperglycemic phase is followed by a phase of hypoglycemia, but their data on this point are not convincing. Trusler et al.,⁹ working with fatally burned dogs, found low blood-sugar values twenty-four hours after burning. Earlier determinations were not done.

Thomsen¹⁰ and Wolff, Elkinton and Rhoads¹¹ have each reported 3 patients with moderately severe burns who showed impaired tolerance for glucose shortly after the injury. There was a gradual return to normal in the course of some days or even weeks.

The most recent study of carbohydrate metabolism following burning has been carried out by Clark and Rossiter.¹² Working with rabbits and rats, under ether anesthesia, these authors found an immediate rise in blood sugar after burning and a return to normal within twenty-four hours. The effect of the anesthetic was controlled. In rats, there was an increased blood lactic acid one hour but not three hours after burning. The blood lactic acid was not studied in rabbits. There was a slight decline in the carbon dioxide combining power in both rats and rabbits. In rats there was a fall in muscle glycogen but not in liver glycogen. In rabbits there was no change in liver glycogen in well-fed animals, but in animals starved for twenty-four hours there was a decrease. Muscle glycogen was not studied in rabbits. Liver slices from rab-

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) and the Burns Assignment of the Surgical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School

The work described in this paper was done in part under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University. Presented, in part, before the meeting of the Subcommittee on Burns and Wound Infections, National Research Council, Washington, D. C., March 31, 1944

†Research associate in medicine, Harvard Medical School, chemist, Thorndike Memorial Laboratory, Boston City Hospital

‡Research associate in surgery, Boston City Hospital

§Laboratory assistant, Thorndike Memorial Laboratory, Boston City Hospital

bits showed an impaired ability to form glycogen from glucose, whereas glycogen breakdown by liver pulp was unchanged.

METHODS OF STUDY

The present report is based on studies of 35 consecutive patients with burns admitted to the Boston City Hospital during the last six months. There were no known diabetic patients in this group. The burns were treated locally with pressure dressings of dry sterile gauze, with no preliminary cleansing. Morphine sedation was given.

Samples of venous blood taken without stasis—usually from the femoral vein—were obtained on admission and at frequent intervals thereafter. The patients were admitted between one and two hours after the burn trauma. Any delay in admission beyond two hours is commented on in the appropriate place in the text.

Blood sugar was determined by two methods—one that of Folin,¹³ and the other a modified Benedict procedure^{14,15} following the removal of proteins by Somogyi's zinc sulfate method,¹⁶ the final dilutions being made in Rothberg Evans tubes.¹⁷ This second procedure greatly lessens the amount of non-glucose reducing substance in the filtrate, a matter of importance in determining "glucose" in the presence of hemoconcentration and hemolysis of red cells.¹⁸

A patient was presumed to have hyperglycemia when the Folin blood sugar exceeded 130 mg. per 100 cc., or the modified Benedict blood sugar 100 mg. Sugar tolerances were determined by the intravenous technic of Lozner et al.¹⁹ Insulin-tolerance tests were made by the intravenous injection of 0.1 unit of regular insulin for each kilogram of body weight. Lactic acid was determined by the method of Barker and Summerson,²⁰ and amino acids by the ninhydrin method of Van Slyke et al.^{21, 22} The carbon dioxide combining power, plasma proteins and chlorides were determined by the usual routine methods, as outlined by Peters and Van Slyke.²³ The serum sodium was determined by the method of Butler and Tuthill,²⁴ as modified by Consolazio and Dill.²⁵ Prothrombin times were determined by a modification²⁶ of Quick's²⁷ method. Cephalin flocculation tests were made by the method of Hanger.²⁸

Shock was evaluated by the usual clinical criteria of fall of blood pressure, high pulse rate, cold, clammy extremities and collapse.

Several patients were treated with therapeutic plasma from the Boston City Hospital Blood Bank. Since this plasma contains glucose in amounts varying from 10 to 17 gm. for each unit of 250 cc., it was necessary to control this factor. This was accomplished in two ways. First, in certain moderately burned patients plasma was withheld; second, other patients were treated with either glucose-free plasma obtained through the kindness of Captain L. R. Newhouser, of the National Naval

Medical Center, Washington, D. C., or glucose-free serum obtained by courtesy of Dr. Stephen Maddock, director of the Boston City Hospital Blood Bank. No protein, fat, carbohydrates or vitamins were given during the period of study, with exceptions that are specifically mentioned below.

RESULTS

Incidence of Hyperglycemia

The over-all admission picture on the 35 patients comprising this study is given in Table 1. Twenty-one patients were in a hyperglycemic state on entry. The initial Folin blood-sugar level varied from 132 to 352 mg. per 100 cc. One patient whose admission was delayed twelve hours had an initial level of 224 mg.

Hemoconcentration was present on admission in 14 patients, 13 of whom showed marked hyperglycemia. Of the 21 patients whose hematocrits were normal on entry, 10 showed a high blood-sugar level on admission. Although there was a close correlation between the incidence of hemoconcentration and that of hyperglycemia, fluctuations in the hematocrit were not, for the most part, paralleled by similar changes in the blood sugar, nor did the non-glucose reducing substances, as a rule, vary directly with the degree of hemoconcentration.

Six patients with burns involving 20 to 75 per cent of the body surface, chiefly of third degree, were admitted in clinical shock. All these patients showed hyperglycemia, the blood sugar ranging from 168 to 352 mg. per 100 cc.

The occurrence of hyperglycemia was directly related to the extent of the burn. Thus, of 9 patients admitted with 2 to 9 per cent of the body surface burned, 2 had hyperglycemia. Of 7 patients admitted with 10 to 19 per cent of the body surface burned, 4 showed marked increases in the blood sugar on admission. On the other hand, 19 patients had more than 20 per cent of the body surface burned, and of these 15 showed marked hyperglycemia.

There is an even more striking correlation of the initial hyperglycemia with the extent of third-degree burn. Sixteen patients were admitted with less than 10 per cent of the body involved with third-degree burns. Of these, 4 showed hyperglycemia, 1 of whom was admitted in shock. In contrast to this incidence, 17 of 19 patients who had third-degree burns on more than 10 per cent of the body surface showed an initial increase in blood sugar. The 2 patients in this group who are not classified as having hyperglycemia had blood-sugar levels at the extreme upper limits of normal.

The data show no correlation of hyperglycemia with previous nutritional status, age, sex or abnormalities in the body temperature on admission.

Duration of Hyperglycemia

The foregoing evidence demonstrates that hyperglycemia occurring shortly after injury is a characteristic finding in severely burned patients. The hyperglycemia persisted over a period of hours in all cases, and over a period of days in some. None of the patients studied showed a return of an

Carbon Dioxide Combining Power and Lactic Acid Level

Plasma carbon dioxide combining power and lactic acid determinations were made on 15 patients. The 4 patients with third-degree burns on less than 10 per cent of the body surface had plasma carbon dioxide combining powers above 20 millimol.

TABLE 1 *Summary of Data*

CASE No	AGE	SEX	NUTRITIONAL STATUS	TYPE OF BURN	EXTENT OF BURN		INTERVAL BETWEEN BURN AND INITIAL BLOOD SAMPLING hr	INITIAL BLOOD SUGAR (FOLIN)	INITIAL HEMATOCRIT	INITIAL SHOCK	OUTCOME
					TOTAL	3RD DEGREE		mg /100cc	%		
1	14	F	Good	Hot aqueous fluid	6	0	3	117	36	0	Living
2	23	F	Good	Flame	30	2	1	127	45	0	Living
3	40	M	Fair	Flame	75	---	2	269	47	+	Died in 3 hr
4	16	F	Good	Hot aqueous fluid	6	0	1	93	38	0	Living
5	8	F	Fair	Hot aqueous fluid	10	---	1	268	38	0	Living
6	45	M	Fair	Hot aqueous fluid	45	---	1	206	65	—	Died in 3 hr
7	49	F	Good	Flame	35	---	12	224	65	—	Died in 7 days
8	1	F	Good	Hot aqueous fluid	4	0	1	112	39	0	Living
9	7	M	Good	Flame	8	2	1	116	40	0	Living
10	54	M	Fair	Flame	20	15	3	201	53	0	Died in 26 days
11	53	M	Good	Hot aqueous fluid	6	0	1	103	40	0	Living
12	1	F	Good	Hot aqueous fluid	2	0	1	138	37	0	Living
13	50	F	Fair	Flame	10	10	2	142	44	0	Died in 11 days
14*	42	F	Good	Flame	75	---	1	202	49	0	Died in 8 hr
15	48	M	Fair	Flame	15	15	1	163	41	0	Living
16	21½	M	Fair	Hot aqueous fluid	20	15	3	168	40	+	Living
17	62	M	Good	Contact hot metal	8	2	1	141	47	0	Living
18	58	F	Fair	Flame	15	10	2½	133	44	0	Living
19	3½	M	Good	Hot aqueous fluid	10	5	1	118	41	0	Living
20	36	F	Good	Flame	35	25	2	130	52	0	Living
21	2½	M	Good	Flame	5	—	1	84	39	0	Living
22	5	M	Good	Hot aqueous fluid	20	0	2	111	41	0	Living
23	5	F	Good	Flame	10	---	1	86	42	0	Living
24	32	M	Fair	Flame	7	3	1	110	47	0	Living
25	12	F	Good	Flame	20	15	1	132	41	0	Living
26	4	M	Good	Flame	50	40	2	347	51	0	Died in 63 hr
27	38	F	Fair	Flame	50	---	2	242	38	0	Died in 63 hr
28*	29	M	Good	Electrical and flame	35	---	1	172	58	0	Died in 22 hr
29*	3	F	Good	Flame	70	---	1½	352	38	—	Died in 6 hr
30	45	M	Fair	Flame	20	15	2	164½	51	0	Died in 5 days
31	75	M	Fair	Flame	20	---	3	109	45	0	Living
32	8	F	Good	Flame	50	---	3	266	56	0	Died in 66 hr
33*	42	F	Good	Flame	15	10	3	100½	40	0	Living
34*	45	M	Good	Flame	60	---	1½	150½	52	0	Died in 16 hr
35	83	M	Fair	Hot aqueous fluid	35	---	2	220½	45	+	Died in 22 hr

* Respiratory involvement

† Benedict blood sugar

elevated blood-sugar level to normal within twelve hours.

The effect of a moderately severe burn on the blood sugar is demonstrated by a study of the data of one patient (Fig. 1).

CASE 18 A 58-year-old woman, with a noncontributory past history, shortly before entry received flame burns on 15 per cent of the body surface, 10 per cent being third degree. The blood pressure and pulse were normal on entry and remained so during the first twenty-four hours. Plasma was withheld and 1500 cc of isotonic salt solution was administered intravenously, but no other parenteral fluids were given. The oral intake during the period of study was limited to water. The urine output was moderately reduced on the first day but became normal thereafter. The blood-sugar level on admission was 133 mg per 100 cc. Thereafter it rose, to a maximum of 238 mg. twenty hours after the burn. By that time the hematocrit, which had been normal on entry, had risen to a maximum of 51 per cent. Thereafter, both the hematocrit and the Folin blood sugar declined, the former reaching a normal value fifty hours after the injury. At that time, however, the blood-sugar level was 162 mg., and seventy-two hours after the burn was 141 mg.

per liter on entry and plasma lactic acid concentrations of between 2.8 and 3.3 milliequiv. per liter. Of the 11 patients with third-degree burns involving more than 10 per cent of the body surface, 6 had carbon dioxide combining powers below 20 millimol. per liter, the lowest value being 13.6 millimol. The lactic acid concentration was between 2.8 and 3.3 milliequiv. in 2 patients, between 4 and 5 milliequiv. in 2, and 6.5 milliequiv. in 8. Thus, as in the case of the initial hyperglycemia, there was a close correlation between the initial decrease in carbon dioxide combining power, lactacidemia and the extent of the third-degree burn.

The following case reports illustrate the course and duration of the changes in lactic acid level and carbon dioxide combining power.

CASE 2 The patient was a well-developed and well-nourished 33-year-old woman with a noncontributory past history who

1 hour before entry received flame burns on 30 per cent of the body surface. For the most part, the burns were deep second degree, only 2 per cent being third degree. The blood

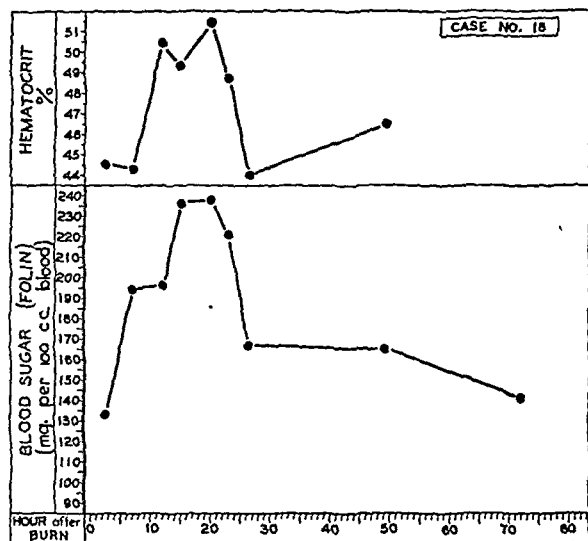


FIGURE 1.

pressure, pulse, temperature and respirations were normal on entry and remained so during the period of study. During the first 24 hours she received 3000 cc. of isotonic salt solu-

tween 35 and 43 mg. during the first 39 hours and fell to 28 mg. at 63 hours.

The blood lactic acid level 2 hours after the burn was elevated to 2.8 milliequiv. per liter. During the next 6 hours it was within normal limits, but during the next 28 hours the concentration varied from 2.0 to 3.9 milliequiv. Further serial studies were not made, but a blood lactic acid determination on the 7th day was normal.

The carbon dioxide combining power of the plasma during the first 63 hours varied between 18 and 24 millimol. per liter. Thereafter, the values remained at 28 millimol. Therefore, during the early period following injury there was apparently a slight but definite decrease in the carbon dioxide combining power.

The blood-sugar level as determined by the Folin method was normal on entry and as determined by the Somogyi-Benedict method was slightly elevated. It gradually rose, the maximum hyperglycemia being observed at 8 hours, with values of 197 mg. by the Folin method and 150 mg. by the Somogyi-Benedict method. The rise in the blood sugar and in the non-glucose reducing substances did not parallel the hematocrit. Thereafter there was a slow decline in the blood sugar over a period of 3 days. No glucose-tolerance tests were done on this patient until the 5th day after the injury, at which time the tolerance was normal.

CASE 13. The patient was a 50-year-old woman whose past history was noncontributory except for moderate alcoholic intake. She received flame burns of 10 per cent of the body surface shortly before entry. The entire burn was deep third degree, the injured skin being completely charred, with fat exposed in a number of places. The blood pressure, pulse and respirations were normal on entry and remained so during the period of study. Fifteen hundred cubic centimeters of physiologic salt solution was given by clysis, but no other parenteral fluids were given. The oral intake was restricted

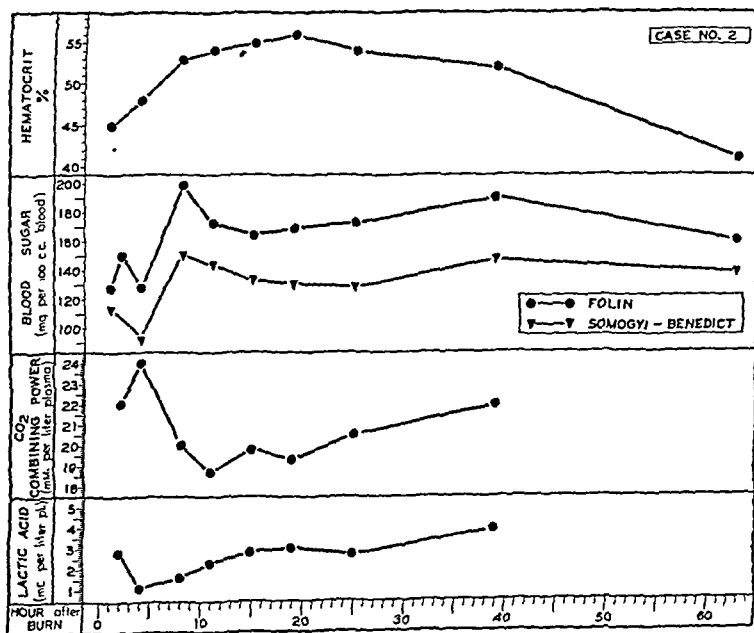


FIGURE 2.

tion by clysis; plasma was withheld, and no other parenteral fluids were given. The oral intake of water and the urine output were low on the 1st day but normal in amount thereafter. The significant laboratory findings are presented in Figure 2.

The hematocrit, which was normal on entry, rose slowly during the first 19 hours, reaching a level of 56 per cent. From then on there was a slow decline to 41 per cent on the 3rd day, at about which level it remained. During that time the plasma protein concentration, which had been normal on entry, gradually fell 4.4 gm. per 100 cc. at the end of 39 hours, presumably owing to a shift of interstitial fluid into the blood stream. The nonprotein nitrogen fluctuated be-

to a small amount of water during the first 36 hours. The urine output was low the 1st day but normal thereafter. The data on this patient are given in Figure 3.

The hematocrit on entry was 44 per cent, at which level it remained for the first 14 hours. There was a slow decline to 34 per cent at the end of 3 days.

The plasma nonprotein nitrogen rose from a level that was initially normal to 75 mg. per 100 cc. 22 hours after the burn was sustained. It declined slowly and reached a level of 39 mg. 65 hours after the injury, at which level it remained. The plasma protein was 6.1 gm. per 100 cc. on entry and declined

slowly to 5.2 gm. in 3 days. On this basis, there was comparatively little interstitial fluid exchange in this patient.

Hyperglycemia, although present, was less marked than in Case 2. The blood sugar rose earlier and reached a peak

moderate and the nonprotein nitrogen remained normal, but a marked hyperglycemia, by both the Folin and the Somogyi-Benedict method, was present. The blood-sugar reached a level of 288 mg. per 100 cc. by the former method

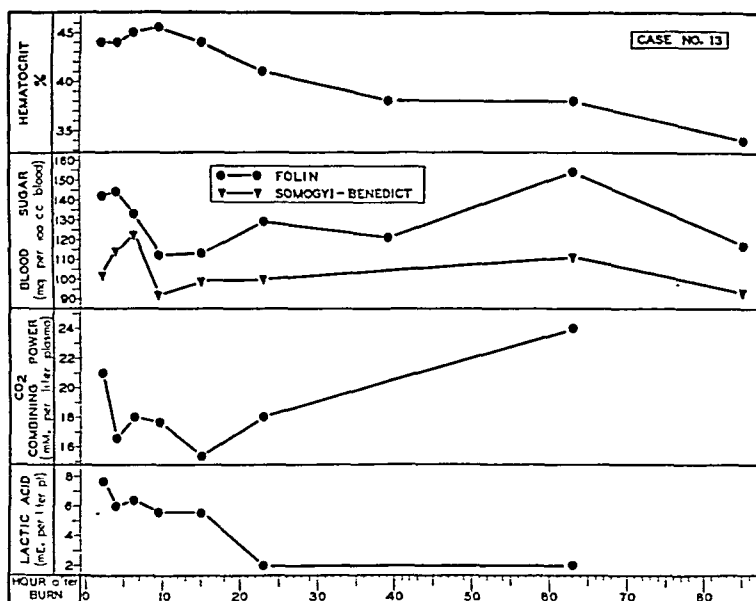


FIGURE 3.

of 144 mg. per 100 cc. by the Folin method and 122 mg. by the Benedict method between 3 and 5 hours after the injury. The level thereafter was normal except for a transitory rise at 62 hours. A glucose-tolerance test done on the 4th day was normal.

In contrast to the relatively slight rise in blood sugar, there was soon after the injury a marked lactic acidemia. On entry, 1 hour after the burn, the blood lactic acid level was six times as high as the normal level, namely, 7 milliequiv. per liter. A high lactic acid level persisted for 14 hours, after which it slowly declined, reaching a relatively normal value in 62 hours.

The carbon dioxide combining power of the plasma, which was 21.4 millimol. per liter on admission, declined to 15.5 millimol. 12 hours later. Thereafter it slowly rose, reaching a level of 26.8 millimol. 62 hours after the burn.

The above two cases are typical of the findings in moderately burned patients, who, in our experience, usually recover from their injury. The following two cases represent patients who had much severer burns and who did not survive the injury.

CASE 14. The patient was a 42-year-old Negress who shortly before entry received flame burns when an oil stove exploded. No further history could be obtained. Physical examination on admission revealed a well-developed and well-nourished woman in moderate distress. The systolic blood pressure was 120, the pulse 90, and the respirations 20. After the burns were dressed it was not possible to take blood-pressure readings, but from the quality of the femoral pulse and the patient's general appearance it did not appear that any profound peripheral failure was present. She died 8 hours after injury from respiratory failure. Fifteen hundred cubic centimeters of plasma, containing about 75 gm. of glucose, was given in the period from 3 to 6 hours after entry. No other fluids were given parenterally or by mouth. There was marked hemoglobinemia. Five hundred cubic centimeters of clear urine was obtained on entry, but none thereafter. The rectal temperature varied from 102 to 102.8°F.

Three sets of observations were made and are summarized in Figure 4. The first two were made before any plasma or glucose had been given. Hemoconcentration was only

and of 241 mg. by the latter at the time of the last observations.

The carbon dioxide combining power of the plasma, which

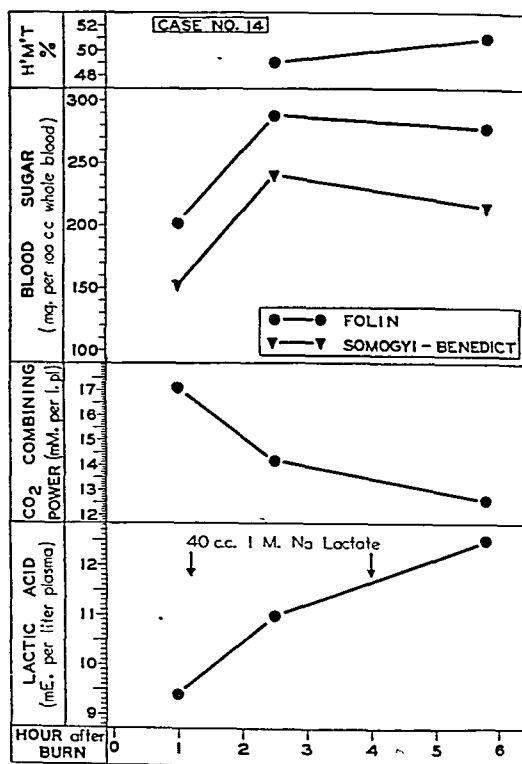


FIGURE 4.

was 17.1 millimol. per liter on entry, fell to 12.5 millimol. in the next 4 hours.

The plasma lactic acid on entry was considerably elevated, a value of 9.4 milliequiv. per liter being obtained. During the next 4 hours the patient received a total of 80 cc. of 1.0 molar lactate and the lactic acid level rose to 12.5 milliequiv.

CASE 29. The patient was a 3-year-old Negress with a non-contributory past history who shortly before entry received third-degree flame burns on 70 per cent of the body surface, together with respiratory damage. Examination on entry revealed a well-developed and well-nourished child who was comatose, with labored respirations. The pulse was 160 and weak, and the extremities were cold and clammy. The clinical condition improved on the administration of oxygen and 600 cc. of plasma. The pulse became stronger and slower and the extremities warm. A Levine tube was passed into the stomach at the 2nd hour after the burn and bloody fluid was obtained. Small amounts of water were administered by gavage. On catheterization at the 5th hour 5 cc. of dark-red urine was obtained. The rectal temperature rose to 105°F. The respirations became more labored, and a tracheotomy was performed 3 hours after injury, with marked alleviation of the respiratory distress. Three hours later, however, the patient suddenly developed respiratory spasm and died.

The hemoglobin varied from 89 to 92 per cent, with the highest value 3 hours after the injury. (These values are higher than those usually found in children in this hospital and probably indicate hemoconcentration.)

The plasma nonprotein nitrogen on entry was 30 mg. per 100 cc. and by the 5th hour had risen to 89 mg.

The carbon dioxide combining power on entry was 13.6 millimol. per liter. During the next 4 hours, 50 gm. of glucose was given intravenously in divided doses. The blood sugar remained at a very high level, the highest value being 700 mg. per 100 cc. 2 hours after the last administration of glucose.

The blood lactic acid on entry was markedly elevated, being 7.2 milliequiv. per liter. Five hours after the burn injury it had risen to 12 milliequiv. No sodium lactate was administered.

Data with respect to glycosuria and acetonuria in the most severely burned patients are not available, owing to the scanty flow of urine during the period of study. Such evidence as is available indicates that there was no change in the renal threshold for glucose. Acetonuria was present in only 2 children, both of whom had normal blood-sugar levels but were moderately dehydrated. With correction of the dehydration the acetonuria disappeared.

Insulin Tolerance

Tolerance to insulin in the early hours following burn trauma was determined in 3 patients. The first patient, (Case 30) was a forty-five-year-old, known alcoholic addict who shortly before entry received a flame burn involving 20 per cent of the body surface, 15 per cent of the burn being third degree. Repeated cephalin flocculation tests were markedly positive, and at autopsy moderately advanced alcoholic cirrhosis was found. The insulin-tolerance test was begun 3 hours after injury, the blood-sugar level being 168 mg. per 100 cc. At that time the lactic acid was 6.6 milliequiv. per liter and the carbon dioxide combining power 19.2 millimol. The blood sugar fell to 108 mg. in one hour, and in two hours had returned to a value of 138 mg.

The other two patients had normal blood-sugar levels at the time the insulin-tolerance test was made. One of these (Case 31) was a seventy-five-

year-old man who had burns on 20 per cent of the body surface, chiefly deep second degree. During the test he showed mild transient shock. The lactic acid level and carbon dioxide combining power were essentially normal. The other patient, (Case 33) was a forty-two-year-old Negress with flame burns on 15 per cent of the body surface, chiefly third degree. The carbon dioxide combining power was also normal, but there was slight elevation of the lactic acid level (4 millimol. per liter). Both these patients showed marked insulin sensitivity five hours after injury. In the first, the control blood-sugar level was 97 mg. per 100 cc. One hour after the injection of insulin it had fallen to 66 mg., and at 2 hours it was still at the level of 60 mg. In the second patient the control blood-sugar level was 98 mg. per 100 cc. One hour after the injection of insulin it had fallen to 49 mg. and by two hours to 39 mg., and at three hours it was still at a low level (24 mg.) Repeated insulin-tolerance tests on the ninth and seventy-seventh days were essentially normal.

Glucose Tolerance

The interpretation of early glucose-tolerance tests in these patients is difficult because of the spontaneous changes in blood sugar. In some of the patients with hyperglycemia, however, it appeared that the added glucose was utilized; that is, the blood sugar two hours after the injection of glucose was the same as, or lower than, the control value. This is illustrated by the following three patients, one of whom was a well-nourished girl who was in good clinical condition at the time of the test. The second was a well-nourished young man in shock at the time of the test, and the third was an alcoholic addict with liver disease but without evidence of clinical shock.

CASE 25. The patient was a 12-year-old Negress with a noncontributory past history who shortly before entry received deep third-degree burns on 15 per cent of the body surface, an additional 5 per cent being involved in second-degree burns. Examination revealed a well-developed and well-nourished girl. The temperature, blood pressure, pulse and respirations were normal on admission. During the first 12 hours the patient received 750 cc. of glucose-free plasma and 360 cc. of water by mouth. There was no vomiting. The urine output was low. The blood pressure remained at about 120/80, the pulse was 110, and the general condition was good. The hematocrit rose from 41 to 47 per cent, whereas the plasma protein concentration remained at about 6.4 gm. per 100 cc. The plasma nonprotein nitrogen rose from 28 to 33 mg. per 100 cc. The carbon dioxide combining power of the plasma varied between 22 and 26 millimol. per liter. The lactic acid was elevated on entry, being 2.3 milliequiv. per liter, but fell to a normal value (0.8 milliequiv.) 12 hours after admission. The blood-sugar level on entry and again an hour later was 124 mg. per 100 cc. by the Somogyi-Benedict method. Twenty-five grams of glucose was injected intravenously at that time, and 2 hours later the blood-sugar level was still 124 mg. Thereafter it was normal. A glucose-tolerance test on the 3rd day was normal.

CASE 28. The patient was a 29-year-old man who received flame and electrical burns and some damage to the respiratory tract. Thirty-five per cent of the body was involved in second-degree and third-degree burns. On entry the blood

pressure was 130/70, the pulse was 100 and of good quality and the respirations were 25. The temperature during the first 5 hours was 103.6°F. Water in sips was the only fluid given. Plasma was withheld. During that time the patient gradually went into profound circulatory collapse, no blood pressure or pulse being obtainable for the last half-hour. There was no output of urine. The hematocrit rose to 72 per cent, and the plasma lactic acid concentration to 5 milliequiv. per liter. The blood-sugar level, which had been normal on admission, rose to 190 mg. per 100 cc. within 1 hour. A glucose-tolerance test was begun at that time. Two hours later the blood-sugar level was 157 mg.

CASE 27. The patient was a 38-year-old woman with probable liver disease who 1 hour before entry received third-degree flame burns on 50 per cent of the body surface. She was a known morphine and alcoholic addict. Physical examination revealed a well-developed and well-nourished woman. The blood pressure, pulse and respirations remained normal during the period of study. The plasma icteric index was 20 to 25 units. There was moderate hemoconcentration, lactacidemia and hyperglycemia. The carbon dioxide combining power varied between 18 and 20 millimeters per liter. A glucose-tolerance test was done at 4 hours. The control blood-sugar level was 286 mg. per 100 cc. Two hours after the injection of the glucose the level was 204 mg.

Glucose-tolerance tests on 4 patients after the fourth day were normal. Two of these patients had shown hyperglycemia, lactacidemia and lowered carbon dioxide combining power during the first two days, whereas the other patients had normal blood-sugar levels but had shown sensitivity to insulin.

Oxygen Consumption

Oxygen consumption was determined in 3 patients (Cases 28, 30 and 33) twelve to thirteen hours after injury. Calculated in terms of basal metabolic rates, the results varied from +34 to +58 per cent. The temperature in each case at the time of the determination was 103°F.

Icteric Index

In 23 patients the icteric indices were normal, whereas in 2 patients (Cases 27 and 30), both known alcoholic addicts, the index was elevated to 12 to 15 and 20 to 25 units, respectively. Of the remaining 10 patients, no data are available on 3; in the 7 others—all with burns involving more than 35 per cent of the body surface—the icteric index could not be estimated because of the presence of marked hemoglobinemia.

Cephalin-Flocculation Test

Serial cephalin-flocculation tests were made on 6 patients, all with third-degree burns involving more than 15 per cent of the body surface. In 3 patients (Cases 31, 32 and 33), the tests were negative, or at the most slightly positive (+). The icteric indices of these patients were normal. In the other 3 patients, 2 (Cases 30 and 34) of whom were known alcoholic addicts, and the third (Case 35) a poorly nourished man of eighty-three, the test was strongly positive (+++ to ++++++) throughout their courses. In two of these patients the icteric indices were not determined because of the presence of hemoglobinemia. In the third patient it was elevated to 15 units.

Prothrombin Time

Serial prothrombin determinations were made on the same 6 patients in whom the cephalin flocculation was studied. Of the 3 with negative cephalin-flocculation tests, 2 (Cases 31 and 33) showed normal prothrombin concentrations and 1 (Case 32) showed slight prolongation eighteen hours after the burn. Of the 3 with positive cephalin-flocculation tests, 2 (Cases 30 and 34) showed moderate prolongation four and forty-one hours, respectively, after the burn.

DISCUSSION

From the data presented it is clear that hyperglycemia, lactacidemia and lowered carbon dioxide combining power are frequently found in human subjects following thermal injury. The extent and duration of the changes in these blood constituents are roughly proportional to the severity of the burn. Muscle and liver glycogen determinations were not made in these patients; however, Clark and Rossiter,¹² working with rats, and Greenwald and Eliasberg,⁸ working with rabbits, found decreases in the muscle glycogen following burns. Clark and Rossiter found no change in liver glycogen in rats and rabbits previously well fed, whereas in rabbits previously starved there was a decrease. Following burn injury, there was no significant degree of early liver damage in those patients treated with simple dressings who came to autopsy in this hospital. The few patients who showed clinical and laboratory evidence of liver damage had a long history of alcoholism and doubtless had liver damage previous to the burn. In 1 patient with such presumptive evidence, the liver was found at autopsy to be markedly cirrhotic. It appears, therefore, that in the presence of a normal liver any increase in lactic acid production due to an increase in the rate of muscle glycogenolysis may result in hyperglycemia. The rate of lactic acid formation following burns is, however, apparently greater than the liver can handle, resulting in lactacidemia as well as hyperglycemia.

In addition to an increased glycogenolysis, another possible source of the extra blood sugar is glucogenesis from protein. It has been shown that following thermal burns there is an early increase in protein catabolism, with the excretion of excessive amounts of nitrogen in the urine.²⁹ It is quite possible that some of this protein is converted to glucose. Another possible factor is the moderate increase in metabolic rate that was found in a few cases in this study.

Hyperglycemia and lactacidemia are not peculiar to burn injury but have been reported following other types of trauma,^{30,31} hemorrhagic shock,³² acidosis,³³ anhydremia³⁴ and low oxygen tension.³⁵ The degree of acidosis, dehydration and oxygen lack

necessary to produce significant metabolic abnormalities, however, is such that these factors can only have been contributory factors in the cases presented here. Similarly, although hyperglycemia has been reported following the administration of morphine,³⁶⁻³⁹ the amounts of the drug required in animals are relatively many times the dosage received by our patients. However, the fact that morphine can cause such a metabolic change should be kept in mind when considering the sedation of burned patients.

The changes in carbohydrate metabolism following hemorrhage are more applicable to the present investigation, since there are certain over-all similarities between burn shock and hemorrhagic shock.

Following hemorrhage, Robertson⁴⁰ presented evidence in cats that the liver is the site of formation of the extra glucose: the sugar content of the hepatic vein blood was higher than that of the heart blood, and ligation of the hepatic vessels prior to bleeding prevented the hyperglycemia. Brooks³² working with chronic spinal cats, showed that an intact sympathetic system is necessary for the production of the hyperglycemia. Of some interest is the fact that Govier⁴¹ was able to reverse some of the effects of hemorrhage on carbohydrate metabolism in cats by the administration of large doses of thiamin chloride.

Most investigators working with burns have emphasized the role of the adrenal glands in the production of abnormalities in the carbohydrate metabolism. Hartman,⁴² working with cats, found an increase in the circulating adrenaline, as measured by the pupil-dilatation test, and a depletion of the adrenaline content of the adrenal glands. Clark and Rossiter¹² have demonstrated some differences between the action of adrenalin and the effects of burn injury. The liver glycogen was increased in animals receiving adrenalin but not in burned animals, and, secondly, liver slices from burned rabbits did not readily form glycogen from glucose in vitro, whereas liver slices from animals receiving adrenalin were able to synthesize glycogen.

Browne⁴³ and Cope et al.⁴⁴ found increased 17-ketosteroid excretion in the first few days following burns, which was followed by a decrease below normal values. Greenwald and Eliasberg⁸ working with rabbits, and Olbrycht,⁴⁵ Weiskotten^{46, 47} and Mallory,⁴⁸ studying patients, have found adrenocortical hypertrophy and a marked depletion of the lipoids. When the burn was severe there was actual necrosis of the cortical cells.

Sayers et al.⁴⁹ state that in burns the adrenal glands are stimulated to exhaustion, and the degree of response is that described in their classification as Type III.

Adrenalectomy was found by Slocum and Lightbody⁶ to prevent the lactic acidemia but not the hyperglycemia in burned rabbits. Clark and Rossiter¹²

found that adrenalectomy did not completely abolish the hyperglycemia and lactic acidemia. It therefore appears that although the adrenal glands may play an important role in the production of abnormalities in carbohydrate metabolism following burns, the entire picture cannot be explained on this basis, and, indeed, the effect of the adrenal glands may be of a secondary nature.

Pathologic changes in other organs following burns have not been consistently found. With conservative surface treatment, which precludes the use of tannic acid and other substances, which have been found to produce focal necrosis, little or no pathologic change in the liver has been observed in our autopsy material. No specific lesions have yet been reported as occurring in the pancreas. The pituitary gland itself has not been studied, so far as an examination of the literature reveals, although Christophe⁵⁰ has described a so-called "burn lesion" in the brain. He found this lesion in the region of the hypothalamus following burning or even after the transfusion of blood from burned animals into the cerebral circulation of a normal animal.

From the foregoing, it appears that there are many possible explanations of the biochemical changes mentioned in this paper. Our own evidence does not permit any statement of the primary cause at the present time. It is not improbable that, whatever the cause is, increased glycogenolysis and possibly gluconeogenesis could have accounted for the findings presented here. It will be necessary to make studies of the actual muscle and liver glycogen reserves of the patients to gain support for this view.

It is already apparent in the small series of 35 patients presented in this report that a marked hyperglycemia associated with lactic acidemia and acidosis go hand in hand with a poor prognosis. So, too, does the counterpart of these findings, namely, the presence of third-degree burns involving more than 25 per cent of the body surface.⁵¹

Although it may be argued that, in general, patients do not die from the biochemical changes reported here, nevertheless the effect of the burn trauma on the organism as a whole must indeed be profound in order to produce such changes in carbohydrate metabolism as are shown in Cases 14 and 29. In any event, from the therapeutic point of view it seems reasonable to suppose that the high blood sugar and lactic acid are obtained at the expense of the carbohydrate reserves of the body. Since in a few of the patients reported here added glucose could be metabolized in the face of a hyperglycemia, it seems reasonable to replace the depleted carbohydrate reserves by the administration of glucose, and to attempt by whatever means possible to increase, in the future, the utilization of carbohydrates by the burned patient. Such a therapeutic approach may well be of benefit.

SUMMARY

In a study of 35 consecutive burned patients, a high incidence of hyperglycemia, lactic acidemia and a moderate reduction in the carbon dioxide combining power of the plasma were found.

There is a high degree of correlation between these abnormalities of carbohydrate metabolism and the severity of the burn.

The few glucose-tolerance tests that were made indicate that in some severely burned patients with hyperglycemia there remains a considerable ability to metabolize added glucose.

There was no evidence of liver damage in these patients as a result of the burn injury. In the few cases in which liver damage was found, it was present before the injury, being for the most part an alcoholic cirrhosis.

Some of the possible physiologic and pathologic bases for the abnormalities of carbohydrate metabolism following burns have been discussed.

The abnormalities in carbohydrate metabolism that have been presented are not inconsistent with the presence of an increased glycogenolysis, together with a possible gluconeogenesis from protein.

It is suggested that additional glucose be given early to burned patients.

We are indebted to Drs. George R. Minot and Charles C. Lund for the interest shown in the development of this work, and to Professor R. A. Peters of Oxford, England, for permitting us to examine the data of Clark and Rossiter prior to publication. The technical assistance of Miss Alice Ballou, Miss Dorothy Keller, Miss Mary Maloney, Miss Jeanette Maioli, Miss Gladys Roberts and Mr. Theodore Kissel is gratefully acknowledged. Dr. George Bottomley kindly permitted us to include Case 32, which was under his clinical care. The clinical and metabolic records were the work of Miss M. Morrow and Miss A. H. MacDonald.

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WAR NEUROSIS*

SURGEON (R) SAMUEL H. EPSTEIN, U.S.P.H.S.†

BALTIMORE

DURING the last world war, military psychiatry constituted a major medical problem.¹ In the course of the postwar years, aggregating nearly a generation, the enormity of the nation's psychiatric problems became obvious to the Veterans Administration, to which the care of the last war's medical problems were entrusted. Since the beginning of the present war, much emphasis has been laid on psychiatry, not only from the standpoint of therapy but also in its preventive aspects. The term "shell shock," coined in the last war, was recognized as a functional nervous disorder and soon gave way to the term "traumatic neurosis of war," a disease in which the trauma was considered to be psychologic. With realization of the heavy burdens carried by the Government with respect to the care of neurotic veterans, medical efforts at the start of the present war were directed toward the screening of psychoneurotics and the early recognition and treatment of the symptoms of war neurosis. The medical literature is replete with contributions by neuropsychiatrists; much has been written on the subject of war neuroses — descriptive, statistical, interpretive and dynamic.²⁻⁷ Most important in medicine, however, is a consideration of the etiology, pathology and therapy of this condition. It is the purpose of this paper to present some observations bearing on these problems.

First, it is necessary to define clearly what is meant by war neurosis and to clear up the terminology by which the topic is bound in the literature. The term "shell shock," already alluded to, proved to be a misnomer. Moreover, it is cogent to point out that the term "neurosis" is not fashionable in military circles because of its effect on the morale of the troops. Thus, the substitution of many different terms occurred, for example, "war fatigue," "exhaustion," "operational fatigue," "combat fatigue," "flying stress," "pilot fatigue," "war nerves," "war weariness" and "war jitters." It is obvious that one must rid oneself of this verbiage in order to have a normal "war neurosis." One must confess that with rabid also is not particularly desirable, because Mallory,⁴⁸ who has little or nothing to do with the cortical hypovivian life.

the lipoids. Over the so-called "war neurosis" actual necrosis of a psychoneurotic history and the

Sayers et al.⁴⁹ essentially stable personality with glands are stimulated to life. Such is usually of response is that desc. neuroses encountered in as Type III.

Adrenalectomy was found in those persons with a body⁴⁸ to prevent the lactacidemia. Society, Baltimore,

* Hospital, Baltimore; assistant
† al, assistant visiting neuro-
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the stresses of combat service, and quite logically are more prone to do so than the non-neurotic are excluded from the group of patients with true war neuroses. The second criterion demands a combat experience of sufficient intensity to precipitate the neurosis. The immediate precipitating factors are of essential significance in this condition, in contrast to the deep-seated psychologic conflicts that are important in the true psychoneurosis unrelated to the war experience. Two other criteria must be satisfied to establish the diagnosis of war neurosis: an acute onset of irritability approximating a constant state of panic, and a relatively quick cure in the acute cases. Thus, war neurosis is a clinical entity characterized by the appearance in a previously stable person of nervous reactions precipitated by a severe catastrophic experience and amenable to quick recovery.

The characteristic symptom of this disorder is the repetitious catastrophic nightmare that has been described in observations of patients in the front lines. This consists of repeated re-enactments of the threatening combat experiences the patient has endured in cumulative fashion. As a result, sleep is disturbed and the patient is harassed by terrifying nightmares. Fear dominates the picture, even in the waking state and, with the increasing fatigue due to insomnia, produces the physical signs of tension and anxiety. The patient usually shows extreme restlessness, irregular tremors, exaggerated reflexes, excessive sweating and a frightened facies resembling the Parkinson attitude. Instead of the anxiety picture, some patients show a listless apathy reminiscent of the affectless schizophrenic.

The so-called "startle reaction" is the second characteristic of war neurosis. Sudden noises, by day or by night, produce in the patient a sudden start, accompanied by the physiologic manifestations of anxiety — tremor, dilated pupils, increased sweating, dry mouth, flushing or pallor and palpitation. No malingerer can successfully imitate this delicate timing of the physiologic effects of anxiety. Not infrequently the startle reaction breaks over into actual panic; the patient runs to the railing of the ship and attempts to jump overboard, screams hysterically or stands transfixed, laughing and crying uncontrollably.

Another sign germane to the clinical picture has been termed "a subtle personality change." The patients become morose, sullen, irritable and intolerant of their shipmates. They do not socialize in a normal way; they seek companionship in drinking; they show indecision and have inner feelings of unrest. It is not always easy to distinguish this personality change from that which accompanies a major psychoneurosis or psychosis. is

to be emphasized that this is not a cardinal sign of war neurosis, and the condition may exist without this phenomenon. There is still a fourth clinical manifestation, also not essential for the diagnosis, namely, a guilt reaction with emotional depression. This is manifest in many survivors of disasters in which a number of the original group were lost.⁸

With this description of the symptomatology of war neurosis, a few illustrative case histories will be presented.

CASE REPORTS

CASE 1. C.B., a 44-year-old, married Coast Guard lieutenant, was admitted to the United States Marine Hospital in a state of severe anxiety characterized by insomnia, terrifying nightmares, tremulous speech with inarticulation and hypersensitivity to noises. He had been in the Navy since 1917 and had served the Coast Guard continuously for the past 20 years. He was on sea duty most of the time, and worked up from the ranks, becoming a senior lieutenant a year previously. He was always in good health, with a stable personality. For the last year and a half he had been on active duty in the South Pacific as chief engineer on a transport ship, working 16 to 20 hours a day in torrid heat, subjected to continual air raids and witnessing the death of his shipmates and even of officers sent to relieve him. During the past few months he had become physically exhausted and had shown signs of dehydration. He felt himself slipping until he could no longer control his nerves. He was unable to sleep, was disturbed by nightmares and was easily startled by the noises in the engine room. While standing watch he was overcome with fear and became tense and tremulous. He was irritable, morose and practically inarticulate, and was finally returned to the United States, arriving in a state of collapse.

When examined on admission a month later, the patient showed a rugged physique, coarse, generalized tremors and an expressionless facies. Speech was inarticulate. He was extremely tense and anxious and appeared to be confused. He realized that his mind was not working well, and he felt utterly hopeless about his future. He was oriented and showed no memory defects. He was still suffering from terrifying nightmares and fear of the slightest noises. This continued during the first part of his hospitalization and was punctuated by startle reactions to the sound of the practice air-raid sirens.

After 2 weeks of intensive treatment with large doses of bromides and chloral hydrate, the patient showed considerable improvement. Psychotherapy was given in the form of reassurance regarding recovery and free discussion of his combat experiences. Sedation was continued for the next 4 weeks in decreasing dosage. After 2 weeks of freedom from symptoms without medication, he was discharged home fully recovered and reported for active duty a month later.

CASE 2. G.S., a 35-year-old merchant seaman who had been going to sea for 12 years, came to the hospital because of severe insomnia of 5 months' duration. He served in the Navy for 4 years and was honorably discharged in 1931. He was always in good health and never showed signs of nervous instability. Since the beginning of the present war he had sailed on tankers. About a year previous to admission his ship was torpedoed twice, and for the first time he became acutely aware of the dangers of the sea in wartime. During his last voyage he was on a freighter carrying a cargo of explosives and traveling without convoy or protecting planes. He began to have vomiting spells, frequency of urination, thumping of the heart and spasms of shaking and was startled by noises.

On examination the patient looked wan and drawn. He showed coarse tremors and hyperactive reflexes. He was tense and apprehensive and admitted that he had been disturbed by the constant threat of danger on the high seas. He talked incessantly about the ship's traveling alone without any protection whatsoever and carrying a dangerous cargo, exposing him to certain death in the event of a submarine attack. He suffered from nightmares of fierce torpedoing of his lone ship.

With heavy and was treated for further

continued for a week he improved
: Maritime Service Rest Center

CASE 3. M.A., a 21-year-old married merchant seaman, entered the Maritime Service Training School a year previously and had been going to sea for the last 5 months. He was the second youngest of six siblings and had an older brother who was also in the service and was injured on the same ship. He attended school up to the seventh grade and after training in a vocational school became a welder. He had had no previous illnesses.

During the last voyage, his ship was torpedoed and sunk, and he was rescued from a life raft by a destroyer and taken to North Africa. He was trembling with fear, was unable to sleep or eat and vomited continually throughout the trip. Whenever a depth charge went off, he became terrified and wanted to jump overboard. On arrival home a month later, he showed the typical symptoms of anxiety. His sleep was disturbed by terrifying nightmares, and his stomach was constantly upset.

On examination the patient showed generalized tremors, vasomotor instability and hyperactive reflexes. He found it difficult to talk, the words sticking in his mouth. He became emotionally unstable when he attempted to describe his terrifying experiences at sea. He admitted that he was more scared than sick, and he could not completely wipe out the memory of his experiences. He was put on sedation and was followed as an outpatient for a few weeks. He received tremendous solicitude from his wife and friends and finally had to be hospitalized on account of an increase in his symptoms.

With mild sedation in the hospital, followed by a period of rest in the Maritime Service Rest Center, the patient's symptoms largely subsided. He was extremely anxious to return to sea with his brother, who had recovered from his injuries.

CASE 4. R.T., a 42-year-old merchant seaman who had been going to sea for several years, and whose ship was torpedoed in January, 1942, continued on duty throughout the following year. He was on a long voyage around Russia and had been blockaded in port there for 10 months. He suffered from inadequate and insufficient food and was greatly disturbed by the tremendously high prices that he had to pay for the necessities of life.

When the patient finally returned to the United States, he became tremulous and fearful and found that he was much dissatisfied with conditions here. He became sullen and morose and took to heavy drinking. He showed extreme hypersensitivity to the slightest noises and was particularly oppressed by practice air-raid sirens. He was unable to sleep and had nightmares picturing life in Russian ports.

On frequent interviews in the hospital, it was learned that the patient had been in rugged health and was extremely fond of seagoing life. He felt acutely the importance of sailing the ships to aid the total war effort. He had numerous complaints about the strategy of the American ships overseas, and could see no reason why he was required to remain completely idle in a Russian port for long periods of time. He showed no physical abnormalities other than general tremulousness and the startle reaction to the slightest noise. He showed considerable bitterness toward the Government for what he considered incompetency in the war plans.

With strong sedation he quieted down considerably, and he was given an opportunity to air his views about the factors of morale in the Merchant Service. After a few weeks he could no longer remain in the hospital and left to return to sea.

CASE 5. G.B., a 23-year-old, married merchant seaman, was seen in the outpatient department in an anxiety state consisting of jittery feelings, sensations of tightness in the stomach, vague pains in the chest and confused thinking.

The patient attended high school and began to work in various factories at the age of 17, and later worked on fishing boats around New York. He joined the Maritime Service in January, 1943. On his first trip the ship was torpedoed and sunk, and he was rescued from a lifeboat by a destroyer, and after a few days was transferred to an American transport and brought home. He had difficulty in sleeping and experienced bad dreams about air-raid bombings and submarine attacks. For a month it was a struggle for him to decide whether or not to return to sea, but he finally decided to do so, since he did not wish to be accused of taking the easiest way out by being drafted. On his next trip in July, after being subjected to repeated bombings from the air, his symptoms increased. After the ship was torpedoed and

sunk, he was rescued and brought home as a passenger on another ship. He was terrified by seeing many of his shipmates killed and others removed to hospitals overseas. He had been home for the last 6 weeks, and had become increasingly worse. His wife noticed that he was extremely irritable and morose, and that he complained of numerous symptoms referable to his stomach. He was startled by the slightest noise and was unable to sleep on account of terrifying nightmares.

On examination the patient showed no physical abnormalities except for general tremulousness. He was mentally clear and talked rationally. He showed some anxiety about the risks of sea duty in wartime, but he felt ready to go back to sea on account of the vital importance of sailing the merchant ships in the war effort.

He was persuaded to go to the Maritime Service Rest Center, where he remained for a short time. He was then advised to take a shore job for a few weeks, and gradually improved, regaining his ability to sleep and losing his stomach symptoms.

As already mentioned, the immediate precipitating factors are of primary etiologic importance in war neurosis.⁹ Nevertheless, a number of environmental factors, physical and mental, must be given consideration in the etiology. These include physical exertion, loss of sleep, insufficiency and irregularity of meals, continued exposure to bodily danger, loss of comrades in death, repeated near escapes from the enemy, frustration of necessary retreat and poor morale. It is not possible to evaluate the number and the severity of the factors necessary to produce a nervous breakdown in any given person, since there is great variability in the response of normal men to stresses. Those encountered in the type of case discussed here are peculiar to war conditions and are characteristically cumulative. It is significant that most of the patients do not break down after the first traumatizing experience, but usually after repeated exposure. This was true of the British experience in the evacuation of Dunkirk, when large numbers of men developed acute war neuroses.¹⁰

It is obvious that physical fatigue plays a large role in reducing the normal mechanisms of defense against emotional disturbance. Fatigue is important not only in land troops but also in men of the naval forces whose rest is usually broken by general alarms, drills, abortive attacks and the like. Fatigue has been such a prominent factor in the etiologic background of these cases that it has been suggested as an alternative term for the syndrome of war neurosis. Physical exhaustion, complicated by varying degrees of starvation, avitaminosis, dehydration and acidosis, is frequently met with.

Of more direct importance in the production of symptoms is the setting of interpersonal relations. In the war situation morale is a potent force in maintaining stability.¹¹ It is often found that the patient entered the combat situation without confidence in his leader. Any incident that strengthens faith in the leader lessens the occurrence of neurotic symptoms. Careful and adequate training is also of great importance in the prevention of war neurosis. It has been repeatedly observed that in the heat of battle men react at an automatic level and

that fear reactions are much less frequent in those performing duties that they know well. Another factor often encountered is the intolerable sense of personal danger felt by a man surrounded by new shipmates whose conduct under fire he has not had time to estimate. He is consequently beset with feelings of doubt and insecurity, adding to the fear reaction.

Other psychologic factors, already referred to, likewise operate through the medium of fear. Prolonged exposure to bodily danger without relief has a tremendous effect on even the hardest of personalities. Repeated near escapes from the enemy and the constant necessity of retreat produce a profound feeling of frustration. The subject is hence unable to discharge his aggression toward the enemy and, witnessing the death of his comrades about him, he becomes paralyzed with fear. These accumulated fear reactions give rise to anxiety and form the essential etiologic basis on which the immediate combat experience operates to precipitate the symptom complex called "war neurosis."

It is now in order to suggest the pathology of this condition by explaining the mechanisms of fear and anxiety in the organism. From the work of Cannon and his colleagues,¹² it is clear that the majority of the symptoms of fear and anxiety are related to the function of the sympathetic-adrenal apparatus. When such a state of sympathetic excitement is long continued, secondary effects result from the glycogenolysis, insomnia, anorexia and hyperventilation that accompany the prolonged adrenal activity. The emotion of fear is a perception in consciousness of these intense and complex somatic changes. In the light of Pavlov's conceptions, this emotion can be considered as a neurochemical reflex that is conditioned by environmental factors to reaction or inhibition by means of various summations, extinctions and facilitations. The fear reaction is a complex reflex, with its efferent arc proceeding through the sympathetic-adrenal innervation from the autonomic centers of the hypothalamus; these in turn are controlled from the cerebral hemispheres, whose function, in the words of Pavlov, is "that of reacting to signals presented by innumerable stimuli of interchangeable signification." Anxiety is an overaction of this fear reflex. By repetition and summation of the stimulus of danger, with constant reinforcement and lack of time for extinction, the reflex becomes either highly facilitated or conditioned to wider and wider associations, until the whole environment becomes an appropriate stimulus of fear. Moreover, analogous to the so-called "analyzer breakdown" of Pavlov's dogs, if the powers of adaptability to danger are overtaxed they may be entirely lost, the fear reaction being left disorganized and uncontrolled. Finally, interference with this mechanism by organic factors of fatigue or disease plays

a part in the cortical breakdown. It may be said, then, that in war neurosis occurring in the setting of continued combat without relief, a dissociation occurs between the cortical activity and the subcortical emotional and vegetative functions.

There are described in the literature other clinical pictures under the heading of war neuroses. They include severe exhaustion states; confusional states varying from mild disorientation to profound delirious reactions with hallucinations; dissociated states, such as amnesias, fugues and localized hysterical phenomena with various visceral disturbances; and acute psychotic and psychopathic disorders resembling the depressions, manic excitements and schizoid reactions. These represent a wide variety of neuropsychiatric conditions and are to be distinguished from the uncomplicated war neurosis. Those cases in which the patients develop complicating symptoms of all gradations of psychoneurosis, psychosis and organic brain disease should be grouped with the classic neuropsychiatric conditions common to civilian practice in which the combat situation is only an incident. In the cases presenting secondary signs, the treatment, prognosis and disposition are exactly the same as those for the same disability occurring in peacetime, except as they may be affected by the secondary gain possible under the pension system to any disability occurring during war. Unfortunately, this has proved to be an extremely serious obstacle in the handling of veterans of World War I.¹³

From the foregoing discussion, it may be seen that war neurosis is a clinical entity with specific diagnostic criteria and etiologic factors, having its pathologic basis in fear. The therapy of the condition is likewise specific. Foremost in importance is the principle of early treatment in the forward areas. The further away from the combat zone the patient is and the longer the treatment is delayed, the poorer is the prognosis. The latest Army figures show that 80 per cent of the patients treated without delay were returned to duty, whereas only 5 to 10 per cent of those evacuated to the rear were cured.

The active therapy is relatively simple and includes two primary considerations: rest and emotional desensitization of the patient to the traumatic combat experience. Rest is obtained by the use of barbiturates to produce profound and prolonged sleep. Supportive treatment with fluids and nourishment should be employed as indicated. Emotional desensitization may be accomplished by simple psychotherapy consisting of reassurance, exhortation, support and encouraging verbalization of the patient's fears. Hypnosis may be used, but deep analysis should be avoided. It is the precipitating factor of the combat situation that is basically significant in war neurosis, and not the unconscious conflicts such as exist in the true psychoneurotic. Group therapy has a place in

dealing with large numbers of these casualties. Another technic of desensitization now in general use consists of allowing the patient to re-enact the frightening memories of his combat experience during narcosis produced by the intravenous administration of amytal sodium. This enables the patient to discharge the content of his fears and recover his amnesias, and to obtain reinforcement through suggestion and reassurance on the part of the physician.

Return to duty should be accomplished as soon as possible, but it is important that the patient be given a certain period of time to "digest" the emotional turmoil before being exposed to another. For this purpose he should have access to a center where directed recreation and physical work are available and simple psychotherapeutic methods are in use. He should be sleeping well, having no nightmares and exhibiting no startle reaction before he is allowed to leave. Those cases requiring further treatment are no longer useful to the service and come under the care of the Veterans Administration, when a well-rounded program of active psychiatric treatment and elimination of the complications incident to continuing disability benefits must be established. This is of vital importance in order to avoid repetition of the governmental burdens of the last war with respect to the care of veterans with neuropsychiatric disabilities.

SUMMARY

War neurosis is a clinical entity characterized by the appearance, in a previously stable person, of fairly constant nervous reactions precipitated by a severe catastrophic experience and usually amenable to quick recovery. The essential etiologic basis lies in accumulated fear reactions amounting to a state of anxiety under continued combat conditions without relief. The mechanism consists of overaction of the sympathetic-adrenal apparatus and the conditioned-reflex reactions of fear, as a result of which a dissociation occurs between cortical activity and subcortical emotional and vegetative functions.

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CLINICAL NOTE

SPONTANEOUS PNEUMOPERITONEUM FROM AN UNKNOWN CAUSE*

REPORT OF A CASE

NATHAN SIDEL, M.D.,† AND
ABRAHAM WOLBARSH, M.D.‡

BOSTON

PNEUMOPERITONEUM may be a spontaneous, diagnostic or therapeutic condition. When it is encountered, except in the form induced for diag-

cording to Hinkel§, the case he reported was the third such report in a review of the literature, and none has been reported since.

CASE REPORT

I. N., a 63-year-old Swede, was admitted to the First Medical Service of the Boston City Hospital on May 1, 1940. There was a 2 weeks' history of an upper respiratory infection followed, 2 days before admission, by a frank chill and pain in the left side of the chest, aggravated by coughing and breathing. The past history and family history were not remarkable.

Physical examination revealed a well-developed and well-nourished male, moderately ill and breathing somewhat laboriously. Except for a reducible right inguinal hernia the positive physical findings were limited to the chest. There was limited expansion of the left chest, with increased

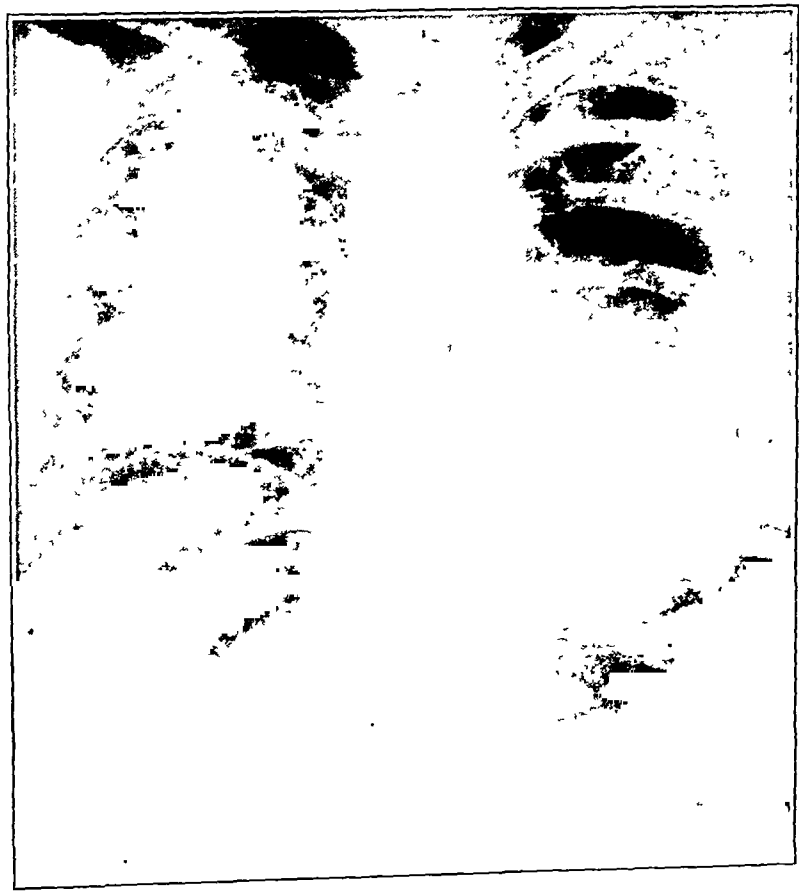


FIGURE 1. Roentgenogram Taken on June 3.

nosis, there is usually some lesion in the gastrointestinal canal as the causative factor. The perforation of a viscus is the usual cause, and in some cases the perforation is a slowly developing leak rather than a sudden puncture.

This case report deals with a rarely reported finding, spontaneous pneumoperitoneum without demonstrable cause and without symptoms. Ac-

tactile fremitus, dullness, an increased whispered voice and a few medium moist rales at the left base. The temperature was 100°F., the pulse 96, and the respirations 26. A diagnosis of pneumonia of the left lower lobe was made and the patient was started on routine pneumonia care and sulpyridine. Both the sputum and the admission blood cultures were reported as positive for Type 8 pneumococcus. Subsequent blood cultures were negative. X-ray examination of the chest the day after admission also indicated pneumonia of the left lower lobe. The patient became afebrile on the 2nd day and remained so the entire 1st week, except for a rise in temperature to 100°F. on the 2nd day. The sulpyridine was discontinued on the 3rd day.

On the 5th day, slight abdominal distention was noted and a few medium moist rales were heard at the base of the

*From the First Medical Service, Boston City Hospital
†Assistant professor of medicine, Tufts College Medical School; assistant visiting physician, Boston City Hospital, associate visiting physician, Beth Israel Hospital
‡Formerly, intern, First Medical Service, Boston City Hospital

§Hinkel, C. L. Spontaneous pneumoperitoneum demonstrable visceral perforation *Am J Roentgenol.* 43 37

lung fields. The distention became progressive and firm. The patient had no complaints except for general discomfort due to the distention. He was given enemas, flaxseed poultices and pituitary extract and rectal tubes were passed, with little reduction in the distention which continued unabated for slightly more than 3 weeks, when it began to decrease progressively. In the 3rd week, because of a continued daily slight rise in temperature and persistence of rales at both bases, another course of sulfapyridine was started and continued for 5 days. The patient again became afebrile for over a week. This was followed by a few days of elevated temperature. From the middle of the 5th week until discharge in the 6th week, he remained afebrile and asymptomatic.

X-ray examination of the chest on the 17th day showed diffuse clouding at the lower half of the left lung field and also a concave shadow at the right base, which was interpreted as being suggestive of a large amount of free air beneath the diaphragm. A flat plate of the abdomen taken on June 3

ination on August 10 (Fig. 2) showed complete disappearance of the pneumoperitoneum.

A review of the past history failed to reveal any abnormal gastrointestinal background. There were at no time complaints referable to the gastrointestinal tract, either during the hospital stay or subsequent to discharge.

Laboratory studies during the hospital stay were not remarkable except for one urine specimen containing sulfapyridine crystals. The stools were negative for occult blood on several occasions. The hemoglobin ranged between 78 and 84 per cent (Sahli) and the white-cell count varied between 7500 and 12,000. The blood smear differentials were normal. A blood Hinton test was negative. The blood non-protein nitrogen on two occasions was 40 and 59 mg. per 100 cc.

It is generally recognized that the demonstration of pneumoperitoneum, except for the form

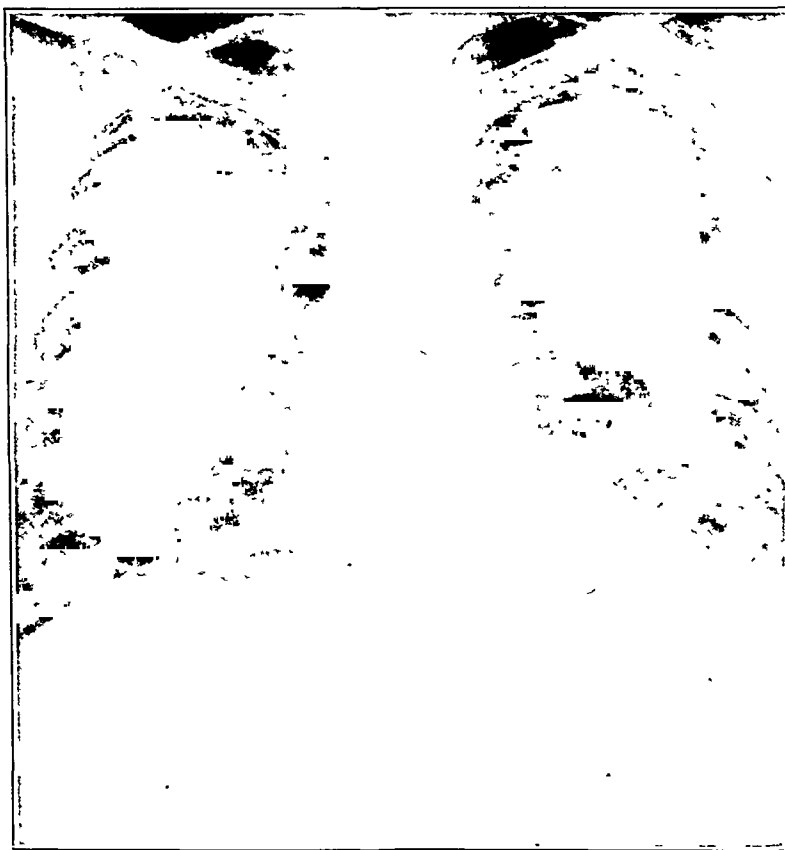


FIGURE 2. Roentgenogram Taken on August 10.

showed an extensive pneumoperitoneum with the liver and spleen outlined (Fig. 1). The abdominal organs shifted with a change in position. Fluoroscopy showed normal movements of both sides of the diaphragm. A barium meal passed normally through the esophagus and entered the stomach without delay. There was no evidence of gastric or duodenal ulcer.

After complete recovery from the pneumonic process and reduction in distention, a gastrointestinal series was performed, which was interpreted as showing hypertrophic gastritis. Lipiodol was injected into the lungs to discover whether a fistula into the peritoneum had occurred through the diaphragm. The results were entirely within normal limits except for slightly thickened pleura on the left. A barium enema was negative. At that time (July 5) the x-ray examination still showed air under the diaphragm.

On July 27 a fluoroscopy of the abdomen demonstrated complete absence of air in the peritoneum. X-ray exam-

induced for diagnostic purposes, is indicative of a perforated viscus due to a peptic, typhoidal, tuberculous or carcinomatous ulcer in the stomach or intestine or to serious abdominal trauma.

Occasionally, pneumoperitoneum is not demonstrable even though a definite perforation in the gastrointestinal tract has taken place as shown at operation or autopsy. When pneumoperitoneum is present, however, one can generally assume that perforation has taken place. Cases are reported of recovery from perforation without surgical intervention and the subsequent disappearance of the pneumoperitoneum, but in these cases a gastro-

intestinal lesion is diagnosed either by x-ray evidence or from the history. In this case, no history or x-ray findings of a gastrointestinal abnormality were obtained, and the patient remained essentially free of abdominal symptoms.

SUMMARY

A case of pneumoperitoneum discovered accidentally during the course of pneumonia without any symptoms referable to the pneumoperitoneum is reported. There was a subsequent spontaneous

disappearance of the pneumoperitoneum. This case is considered unusual because no gastrointestinal abnormality was shown by the history, laboratory tests or x-ray investigation. There was x-ray evidence of the marked pneumoperitoneum and the complete disappearance of such findings after a three-month interval.

The possible relation of a pneumoperitoneum to the pneumonic process by the formation of a fistula was investigated, but no basis for it was discovered.

MEDICAL PROGRESS

MODERN CONCEPTS OF RENAL STRUCTURE AND FUNCTION IN CHRONIC BRIGHT'S DISEASE (Concluded)*

STANLEY E. BRADLEY, M.D.†

BOSTON

FUNCTION

During the past year Smith^{42, 43} has published an engaging and intimate account of the development of the modern concepts and methods of renal physiology. As he points out, the modern era began with the appearance of Cushny's⁴⁴ monograph, *The Secretion of Urine*, and the promulgation of his "modern view." Cushny succeeded in establishing order and coherence among the mass of data that had accumulated by rejecting all of the many existing theories and postulating but two renal excretory activities—glomerular filtration and differential tubular reabsorption. The introduction of the microcapillary pipette by Richards⁴⁵ to obtain samples of glomerular filtrate and tubular urine directly for analysis firmly established the doctrine that the glomerular filtrate is a simple ultrafiltrate of the plasma. Although the early work was done on cold-blooded animals, recent work has extended the direct proof of the validity of this hypothesis to mammals.^{46, 47} For many years the influence of Cushny's ideas and the absence of solid evidence excluded the possibility of tubular excretion, but in 1923, Marshall and Vickers⁴⁸ showed that phenol red was excreted by the kidney even when the perfusing pressure was too low to permit filtration. Moreover, they noted that more phenol red appeared in the urine of the normal animal than could possibly be excreted by filtration alone since most of the dye is bound to the plasma protein leaving only a small fraction available for filtration. Therefore, it seemed reasonable to conclude that a process of

active tubular excretion must be concerned in the renal elimination of phenol red. To this evidence were added supportive data derived from a study of aglomerular fish.³⁵ In these animals urine is secreted in the absence of a filter bed and all the constituents that may be found in urine, save protein, glucose and ferricyanide, are voided. It soon became evident that quantitative study of tubular excretion and reabsorption could be possible only if a means of measuring the rate of glomerular filtration could be devised. Filtration rate could then be used as a standard of reference, since the excretion of any substance in excess of the amount filtrable would indicate a contribution by the tubules, and conversely any deficit would indicate net reabsorption.

Clearances

Quantitative studies of renal function began with studies of urea excretion and led to the development of the clearance concept. When Van Slyke first introduced the term "clearance" he had reference to the virtual volume of blood completely cleared of urea in each minute by the kidney, but as Smith⁴² points out, the term has acquired broader meaning in recent years and "taking conceptual wings, has become a generalized notion applicable to all aspects of renal excretion." The first concept of the urea clearance was confused by the introduction of a square-root radicle into the term at low urine flows, "a mathematician's device to squeeze a correlation out of data in which a simple correlation is not present."⁴² Once it was appreciated that the use of the square-root radicle had no physiologic justification, the situation was simplified: the clearance term could be applied to any substance, and the ratio between the quantity of the material

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Instructor, Department of Medicine, Boston University School of Medicine; assistant physician, Evans Memorial, Massachusetts Memorial Hospitals.

excreted each minute and its concentration in plasma or blood could be expressed in terms of a volume of plasma or blood cleared of it per minute. If a substance is to be used in measuring filtration rate it must be excreted only by filtration. The quantity cleared is the amount contained in the plasma that passes through the filter; its plasma clearance is equal to the filtration rate. In a phlorizinized animal, glucose is no longer reabsorbed and since there is no tubular excretion of this substance, it follows that, in this situation, the glucose clearance must be equal to the filtration rate. It has been found that glucose clearance in the phlorizinized animal is equal to the clearance of inulin, mannitol, sorbitol or dulcitol when these determinations are made simultaneously.⁴² In the normal animal and in man, the clearance of glucose is zero, whereas the values for the other substances are identical with those in the phlorizinized animal. Hence there is good evidence that these substances can be used to measure filtration rate.

If all the blood passing through the kidney is completely cleared of a given substance, then the measurement of this clearance is equivalent to the measurement of blood flow. Among substances found to be approximately so cleared are Diodrast and sodium para-amino hippurate. Of course, one would not expect absolutely all the blood flowing through the kidney to be cleared, since a portion of it perfuses nonexcretory tissue. Nevertheless, recent determinations of the renal extraction ratio of sodium para-amino hippurate reveal that 90 per cent of the material, on the average, is removed on one circulation through the kidney.^{41, 49} Therefore it seems fair to assume that the clearance of this material (and of Diodrast) is a measurement of the blood perfusing functional excretory tissue, that is, of effective renal blood flow.

With such methods for measuring glomerular filtration rate and renal blood flow, students of renal physiology and disease have been able to move on to quantitative studies of renal hemodynamics and tubular activity. For example, the ratio between filtration rate (GF) and blood flow (PF), namely, the filtrate fraction (GF/PF), is the percentage of the renal blood flow filtered at the glomerulus. This value is a function of a number of variables, including intraglomerular pressure, plasma oncotic pressure, intrarenal pressure and the viscosity of the blood. Smith and his associates⁵⁰ have undertaken an analysis of these variables with the aim of ascertaining the relative effect of vasomotor activity in the afferent and efferent glomerular arterioles. They showed that similar changes in all values result from afferent arteriolar control of blood flow, that is, a fall in GF, PF and filtrate fraction during increased afferent resistance, and a rise in all with decreased afferent resistance, whereas a constant filtration rate is maintained over a wide range of renal blood flows by efferent arteriolar

control of intraglomerular pressure. Since the filtration rate tends to remain constant in normal animals and man, and also in hypertensive patients with a wide range of decreased renal blood flows, they concluded that the prime determinant of glomerular dynamics is efferent vasomotor activity. Lampport,^{51, 52} however, in a subsequent analysis of the same data took issue with this conclusion. On the basis of formulations of afferent and efferent arteriolar resistances derived from Poiseuille's law, he deduced that both sets of arterioles must be active to maintain a constant filtration rate since, contrary to Smith's hypothesis, his calculations showed that efferent control would be expected to change filtration rate from zero at low blood flows to a maximum at normal flows and back to zero at high rates of renal blood flow, an obviously impossible physiologic situation. Shannon,⁵³ on the other hand, criticizes both hypotheses for their dependence on assumed constant values for immeasurable variables and points out that Lampport's treatment does not recognize the importance of the elastic resistance of the glomerular capillaries. Lampport⁵⁴ admits the justification of the first criticism, but claims that his calculations are flexible enough to account for all conceivable factors. The fundamental difference between these two hypotheses can best be seen when they are applied to an interpretation of the hemodynamic events of essential hypertension. Early in the course of this disease, the filtrate fraction increases as a result of the diminished blood flow through the kidney without significant change in the filtration rate. Smith⁵⁰ places the site of the vasoconstriction responsible for the decreased blood flow in the efferent arteriole, whereas Lampport⁵⁵ believes that the resistance in both arterioles is increased with afferent outweighing efferent vasoconstriction. Undoubtedly further analysis will resolve the differences between these two points of view.

The application of the clearance methods to the measurement of the dynamic activities of diseased kidneys has been severely criticized because of the over-all character of clearance measurements.⁵⁶ Thus the demonstration of hypertrophy and atrophy in the same kidney implies a compensation on the part of some units for the decreased function in others, allowing the average function of the two categories measured by clearances, to remain unchanged in spite of the marked local alterations that have occurred. This type of behavior has been demonstrated functionally, as well as anatomically, in dogs with chronic interstitial nephritis. These animals have been shown to handle a dye, trypan blue, in a manner different qualitatively and quantitatively from the normal since it appears that filtration with or without reabsorption and actual diffusion into the tubular lumen may take place. It is asked, then, Why may there not be a similar change in the manner in which inulin is excreted,

making it unsuitable as a measure of the filtration rate? Furthermore it has been shown that renal tubules severely damaged by uranium cease to excrete Diodrast and they allow inulin to diffuse back into the blood.⁵⁷ These criticisms appear to have been answered satisfactorily.⁵⁸ It is admitted that the clearances are average figures but, that, considered in relation to the total mass of active tubular tissue, they continue to have significance in assessing the relative changes in filtration rate and renal blood flow. Furthermore it has been demonstrated that the clearances of inulin and mannitol in glomerulonephritis,⁵⁹ eclampsia⁶⁰ and the profound renal hemodynamic changes of shock⁶¹ are in agreement. If molecular diffusion in either direction between the tubular lumen and the blood occurred, then agreement of these values could not be expected, since the rates of diffusion would not be equal for such dissimilar molecules. It is immaterial for the measurement of blood flow how Diodrast or para-amino hippurate is excreted, provided the blood is entirely cleared. In renal disease, blood perfuses a smaller and smaller mass of excretory, relative to nonexcretory, tissue and as a result, the over-all extraction ratio would be expected to decrease. Obviously, with extreme damage the Diodrast (or hippurate) clearance fails to measure even approximately the actual renal blood flow. As a matter of fact, extraction ratios as low as 55 per cent have been observed in a case of chronic diffuse glomerulonephritis in the nephrotic stage when over-all renal function was not greatly impaired.⁴⁹ This does not mean, however, that in such cases these clearance methods should be discarded as valueless. They continue to measure the blood flowing to residual functional excretory tissue, since it is unlikely that at the low plasma levels of Diodrast (or hippurate) employed the capacity of any perfused functioning tissue is exceeded. This surmise is strengthened by the demonstration that the proportionality between the amount removed by and the amount offered to the kidney at progressively higher plasma levels remains unchanged and normal in pattern until very late in the course of glomerulonephritis.⁵⁹ This indicates that the functional tissue is handling the substance in a normal fashion and that the Diodrast (or hippurate) clearance, in these circumstances, is a valid measure of blood flow to such functional tissue.

Tubular Function

The necessity of relating the renal blood flow to the mass of functional tissue became obvious when the problems of ischemia and hyperemia, of hyperfiltration and hypofiltration in residual glomeruli and of hyperfunction and hypofunction in variously damaged tubules were considered. To understand the methods used for assaying the mass of renal functional tissue one must return to the question of

tubular reabsorption and excretion. Given a method for determining glomerular filtration, the role played by the tubules in the renal secretion of a given substance can be accurately quantitated, for example, at high plasma levels of glucose the amount of tubular reabsorption of glucose is equal to the amount filtered less the amount that appears in the bladder urine. Early in the study of tubular function it became apparent that many substances, particularly nonelectrolytes, were handled by tubular transfer mechanisms of definitely limited capabilities. For example, glucose is entirely reabsorbed from the glomerular filtrate until the load exceeds the capacity for reabsorption, when reabsorption continues at a fixed maximal rate while the excess is spilled in the urine. Similarly the excretion of Diodrast is limited by the maximal capacity of the tubules to handle it. Such maximal rates of either reabsorption or excretion are functions of the quantity of active tubular tissue. After unilateral nephrectomy the maximal rates are approximately halved,⁶⁴ and with the succeeding hypertrophy of the remaining kidney they slowly increase. Moreover, it has been shown that a clear-cut correlation obtains between glomerular filtration rate and maximal tubular activity (Tm) and that a similar relation holds for blood flow and Tm.⁶² The wide variability of the discrete functions in persons of varying size vanishes when the clearance values are expressed in terms of these factors. Hence, in disease where all functions may be depressed, a knowledge of the *effective* renal blood flow of itself may be of no value in estimating the presence of renal ischemia or hyperemia, but when related to the mass of residual functioning tissue, it may give helpful information regarding these matters.

Saturation methods, such as those used in the determination of transfer maxima, have been applied to an analysis of the distribution of glomerular and renal vascular dysfunction^{43, 63} and have, under certain circumstances, indicated the presence of co-existent hyperfunction and hypofunction. Shannon and his associates⁶⁴ have shown in the normal dog that glycosuria occurs abruptly and that all the nephrons apparently are simultaneously saturated (glucose Tm is reached) at a given level of plasma glucose. This requires a nice adjustment between the individual glomerular filtration rates and the capacity of the attached tubules to reabsorb glucose and implies an anatomic and physiologic correlation between the size of the glomerulus and its attached tubule such that the large glomeruli are attached to large tubules and small glomeruli to small tubules. If this adjustment did not obtain, glucose would begin to appear in the urine at plasma levels of glucose lower than those required to saturate all the nephrons, because at such low levels the maximal rate of reabsorption would be reached in tubules getting a larger proportional quantity of filtrate. Almost the same situation has been

found in man for both glucose and Diodrast.⁶³ With respect to the latter, the phenomenon indicates a proportional distribution of blood flow to every tubular excretory cell. Owing to this fact, a progressive elevation of the plasma level (so-called "titration" of the kidney) of either Diodrast or glucose is associated with an equal increase in the amount transferred by the tubular cells until Tm levels are reached, when the transfer rate abruptly becomes constant. This proportionality between the load and the transfer rate may be disturbed by disease. Hyperemia of some of the nephrons results in relatively higher perfusion and filtration rates allowing saturation of these units at low loads; whereas ischemia has a reverse effect. Mathematical and statistical analyses of the defects in proportionality have been published in the past year, and distribution curves for relative glomerular activity and tubular perfusion have been derived for normal kidneys.⁶³ These methods have also found application in the study of the kidney of essential hypertension.

Before turning to the application of these methods to the study of renal physiology in chronic Bright's disease, certain aspects of recent studies of tubular function must be considered with special reference to their bearing on renal disease. The discovery of maximal transfer capacity permits examination of the intracellular mechanisms by which these tubular activities are carried out. Thus, the effect of the presence of other substances that may interfere with enzymatic activity or that may enter into the reactions by which transfer is accomplished can be studied and inferences may be drawn concerning the nature of various intracellular metabolic processes. This is an extremely important consideration, since renal hypertension and other effects of renal dysfunction may arise from a derangement of intracellular activities of the tubular cells.⁶³ Shannon,⁶⁵ in an important review of this subject, has shown that the available data are consistent with an explanation of the phenomena of limited transfer in terms of the mass-action law, assuming the intermediacy of a transfer substance. During the past year, Pitts^{66, 67} has reported the results of a study of the reabsorption of various amino acids and suggests certain modifications of Shannon's hypothesis, which are necessary to explain the kinetics of amino acid transfer. It is interesting that several substances appear to compete for excretion or reabsorption by the same mechanism. Several different series of such substances have been studied. Glucose, xylose, galactose and sucrose are apparently reabsorbed through the agency of one transport system,^{63, 68} whereas phenol red, Diodrast, Hippuran,⁶⁹ Iopax, Neoipax, Skiiodan,⁷⁰ para-aminohippuric acid⁷¹ and penicillin^{72, 73} are excreted by another mechanism. In the case of the first system, preferential treatment is given to glucose, which, when present in sufficiently large

amounts, excludes other members of the group from transfer. In the second series, Diodrast appears to be preferentially excreted and glycine heads a series of amino acids, including alanine, glutamic acid and arginine,⁶⁷ that are reabsorbed preferentially in the order named. The action of phlorizin has been interpreted by some workers as an effect of competition with glucose for an intracellular transport system,⁵³ although there is evidence that it produces its effect by interference with the action of kidney phosphorylase.⁷⁴

Many tubular activities, such as water reabsorption and sodium or potassium transport, are known to be under endocrine control. It has recently been demonstrated that the hypophysis, adrenal cortex, gonads and thyroid gland are capable of affecting tubular transport systems. Hypophysectomy is followed by a decrease in Diodrast Tm and by a failure of hypertrophy to occur in the remaining kidney after unilateral nephrectomy.^{75, 76} The administration of thyroid causes increased Diodrast transfer in animals.⁷⁷ Estradiol depresses the absorption of ascorbic acid⁷⁸ and causes renal hypertrophy, possibly on the basis of interstitial edema.⁷⁹ Testosterone administration is followed by hypertrophy of both kidneys in experimental animals⁷⁹⁻⁸² and an augmentation of Diodrast Tm.⁸³ For this reason it has been suggested that the trophic effect of testosterone might prove of value in stimulating hypertrophy of residual renal tissue in the course of Bright's disease.^{81, 84} Furthermore, it was thought, that the retention of nitrogen due to increased protein building supposedly induced by testosterone administration, might serve a useful purpose in patients with nephrosis losing large amounts of protein.⁸⁵ Two cases of renal disease have been reported in which therapy was based on this rationale.^{82, 85} There is no evidence of benefit. In Cushing's syndrome due to adrenocortical tumor, no change in Diodrast Tm or Diodrast or inulin clearance was noted by Barnett and his co-workers.⁸⁶ Moreover, Heinbecker and his group⁷⁷ failed to find any renal change following the administration of cortical extract to dogs, and desoxycorticosterone, in the hands of Winkler and his colleagues,⁸⁷ failed to produce any noticeable effect during anuria. The experiments of Selye and his co-workers,⁸⁸⁻⁹³ however, revealed a profound change in the kidneys of experimental animals following the administration of desoxycorticosterone. These investigators discovered that this substance produced renal lesions in the chick resembling in every way nephrosclerosis,⁹² but it was also found that excess salt ingestion produced similar lesions.⁹³ An extension of the study to mammals (dog, rat and monkey) disclosed that desoxycorticosterone overdosage combined with the ingestion of large amounts of sodium chloride produced renal lesions similar to those of malignant nephrosclerosis in man.^{88, 89} Accompanying the development of the renal lesions

the blood pressure rose to hypertensive levels and death occurred on the basis of renal insufficiency and cardiac failure. Vascular lesions were found not only in the kidney but also in the pancreas and in the adrenal capsule. Recently it has been found that the action of desoxycorticosterone in the experimental animal may be completely blocked by methyl-testosterone.⁹⁴ What bearing these discoveries may have on the question of the etiology and therapy of human malignant nephrosclerosis remains to be seen.

Despite the sensitivity of tubular activities to many extrarenal influences, values of Tm in normal animals and man are strikingly constant and reproducible.⁶³ The maximal tubular transport rates of glucose and Diodrast have been shown to be constant and independent under a variety of experimental conditions. The administration of adrenalin and caffeine and the induction of renal hyperemia during pyrogenic reactions do not affect the values of glucose and Diodrast Tm to any significant degree.

The constancy of glucose Tm has important theoretical consequences. It has long been known that only a portion of the glomeruli are active at any one time in the amphibian kidney, and it has been supposed, on the basis of injection studies,⁹⁵ that a similar inactivity of an appreciable number of glomeruli may occur in the mammalian kidney. It has been assumed that caffeine diuresis in man follows induced activity of previously inactive glomeruli, which direct observation has shown to be the case in the frog. If this were true, a marked increase in filtration rate and in glucose Tm would be expected after the administration of caffeine because the opening up of nonfunctioning glomeruli would bring into operation nephrons previously not filtering and reabsorbing glucose, thus causing an increase in maximal reabsorptive capacity. This does not happen. On the other hand, adrenalin might be expected to shut down a number of glomeruli and to reduce Tm. Forster⁹⁶ has shown that this is the case in the frog, where glomerular intermittency can be directly observed, but no change in Tm occurs in man.⁶³ Hence, the facts "controversy the idea, carried into mammalian physiology from observations on cold-blooded animals, that any significant number of glomeruli are inactive at any moment."⁶³ In addition, direct observation of mammalian glomeruli has failed to reveal any evidence of glomerular intermittency.⁴⁷ Explanations of drug action in man based on this hypothesis must be discarded. Obviously the concept of a glomerular reserve is unfounded and the filtration rate may be taken as a measure of the filter bed.

Functional Patterns of Disease

Renal function in 22 patients in various stages of glomerulonephritis has been studied by the methods

outlined above at the Welfare Island Hospital in New York City by Earle, Taggart and Shannon.⁴¹ The earliest manifestation of the disease was an interference with the glomerular filtration rate, as one would expect on the basis of what is known of the pathology. In addition to the fall in filtration rate, renal blood flow increased or it remained at a normal level. As a result, the filtration fraction decreased from a normal level of 19 per cent to as low as 8 per cent. It is known that afferent vasoconstriction may lower intraglomerular pressure, with a fall in filtration rate and filtrate fraction. This appears to be the case in shock^{61, 97} and in chronic anemia,⁹⁸ both of which are accompanied by a decreased renal blood flow. Since in glomerulonephritis, however, the blood flow may actually increase, it appears likely that the decreased filtration rate and filtration fraction found in glomerulonephritis are attributable to impairment of filtration caused by the action of the disease on the glomerular membrane.

At first there seemed to be relatively little interference with tubular function, and it was pointed out that the resultant loss of the normal adjustment between glomerular filtration rate and the functional capacity of the attached tubule may have serious consequences, since "glomerular damage out of proportion to the impairment of tubular function should predispose to the retention of electrolyte and, incidentally, water, as is so common."⁵⁹ With progression there was a destruction of tubular tissue roughly parallel to the reduction in filtration rate, as evidenced by the fall in the Diodrast Tm. Here too, however, there was relatively greater reduction in filtration rate than in tubular mass so that the glomerular filtrate-Diodrast Tm ratio (GF/Tm) remained depressed and glomerulotubular imbalance continued to be prominent. At first blood flow was well maintained, but when the Tm was reduced to half normal, the blood flow was consistently reduced to extremely low levels. It should be noted that high blood flow-Diodrast Tm ratios (PF/Tm), denoting relative hyperemia, were not uncommon in any phase of the disease.

The low filtrate fraction remained prominent during the entire course until the appearance of hypertension or the extreme reduction of Tm in the terminal stage either considerably altered glomerular dynamics or so invalidated the measurement of blood flow that the filtrate fraction rose to normal or high levels. At that time too, there was often a reversal in the glomerular filtrate-Diodrast Tm ratio (GF/Tm). Hypertension was not necessarily related to the extent of tubular damage, although it seemed to be consistently present when Tm had been reduced to one quarter normal. During the acute stage and in acute exacerbations of the chronic disease a reduction was observed in filtration rate, Diodrast Tm, and GF/Tm, followed by a return toward the normal levels during recovery, but no

correlation was apparent between the gravity of these changes and the ultimate course of the disease. Occasionally the values returned to normal while proteinuria was still obvious. Two findings stand out in this study, namely, the predominance of glomerular impairment and the appearance of relative renal hyperemia throughout the course of the disease. These features are consistent with the pathology and with the belief that glomerulonephritis is pre-eminently an inflammatory disease.

The functional pattern of glomerulonephritis stands in striking contrast to that found in the course of nephrosclerosis. Sixty subjects with essential hypertension were examined by Goldring, Chasis, Ranges and Smith.⁹⁹ Early in the disease changes in filtration rate and renal blood flow appeared to be based upon hemodynamic rather than upon organic changes. The filtration fraction was increased as a result of decreased blood flow in the presence of an unchanged filtration rate. The authors are of the opinion that this pattern is caused by efferent arteriolar vasoconstriction that is functionally reversible (hyperemia followed the administration of pyrogenic inulin with a fall in the filtration fraction) and that it is not dependent on neural pathways (the pattern remained unchanged after extensive sympathectomy) and is therefore probably attributable to the activity of some unknown humoral agent. With progression of the disease there was a steady loss of tubular tissue manifest in the gradual reduction in Diodrast Tm, a loss that at times outran the impairment of filtration, thus indicating the presence of impotent tubules or possibly increased pressure in the glomerulus as a result of increased systemic arterial pressure. Whereas the glomerular filtrate-Diodrast Tm ratio (GF/Tm) tended to increase, unlike the situation in glomerulonephritis, the renal blood flow-tubular excretory mass ratio (PF/Tm) ranged from low normal to very low values, thus indicating relative renal ischemia. A study of the distribution of blood to its tissue substrate during hypertensive disease, however, revealed fairly uniform spread even when the disease was so far advanced as to distort markedly the anatomy and the delivery of filtrate.⁶³ Focal renal ischemia appeared to be the exception rather than the rule in this disease. The slight increase in Diodrast Tm that often followed the administration of pyrogen might have been evidence that in some cases highly ischemic tubules were brought into perfusion by hyperemia. The distribution of glomerular filtrate to tubular reabsorptive mass (glucose Tm), on the other hand, showed a marked distortion with a tendency for the over-all filtration rate to remain within normal limits, owing to the opposing operation of large numbers of hyperemic and ischemic glomeruli. It is interesting that the earliest, most persistent and most consistent finding in the hypertensive kidney was a reduction in Diodrast Tm, usually considerably in excess of the

glucose Tm. This finding indicates that two activities presumably localized in approximately the same segment of the nephron may be affected differently by the same disease process. Glucose Tm fell only after a considerable change in Diodrast Tm had occurred, and it was thought that this preferential depression of the rate of Diodrast excretion might arise out of an interference by the disease with intracellular metabolic activities and indeed might point to the primary defect in the kidney in essential hypertension.⁶³ In summary, the renal functional picture during the course of essential hypertension seems to be one in which the progressive reduction in Diodrast Tm is associated with a reduction in renal blood flow, little or no change in filtration rate and an elevation in the filtrate fraction, all of which are probably attributable to the hemodynamic factor of increased arteriolar tone (predominantly efferent). There is little alteration in the distribution of blood to each unit of the parenchyma, but a marked distortion in the distribution of filtrate to the tubules, probably again on a hemodynamic basis, so that hyperfiltration in some units balances hypofiltration in others and maintains an over-all filtration rate within normal limits.

Renal functional patterns have not yet been clearly defined in the nephroses. A number of the patients studied by Earle and his co-workers⁶⁹ were examined during the nephrotic stage of glomerulonephritis. There were no distinctive features by which these patients could be distinguished from others suffering from chronic diffuse glomerulonephritis. In nephrotic children, however, it has been known for several years that the urea clearance is increased.¹⁰⁰ The inulin clearance has been found to be elevated as much or more than the urea clearance,¹⁰¹ and during the last year Emerson and Dole¹⁰² reported increases in both inulin and Diodrast clearances with a slight elevation of the filtration fraction. They attribute the supernormal urea clearance to increased renal blood flow.

* * *

Obviously a considerable amount of work remains to be done. Knowledge of functional patterns during chronic Bright's disease is faulty and incomplete. Although many new methods have been developed by which quantitative studies of renal activities may be made, they have found intensive use only in the study of glomerulonephritis and of essential hypertension. Pyelonephritis and the various nephroses await similar investigation. These studies are of the greatest importance from the standpoint of pathogenesis, diagnosis, prognosis and treatment. The discovery that certain functional hallmarks distinguish glomerulonephritis and essential hypertension may find use in differential diagnosis. Further special investigations may reveal facts on which prognostic criteria can be safely established. Elucidation of the etiology of chronic Bright's disease, clarification of the difficult prob-

lems of hypertension and improvement of therapy may result from an intensive examination of tubular intracellular metabolic activity.

65 East Newton Street

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-THIRD ANNIVERSARY

House of Delegates, May 15 and 16, 1944 (Continued)

The next report was that of the Committee on Child Health, by Dr. Fairfield, as follows:

We recommend that the infant-care portion of the Emergency Maternal and Child Care Program be accepted under the following conditions:

That major surgical aid not be included, again because of the difficulty in determining who are "qualified consultants."

That medical aid be accepted only for illnesses requiring over two home or office visits. (This plan would eliminate many needless calls on essentially well babies and would eliminate a great deal of extra work involved in applying for aid, authorizing the service and approving the records for payment.)

Dr. Mullins asked whether he was correct in saying that the maternity program was not tied up directly with the maternity program previously voted on. Dr. Atchison replied that the program did not have to be accepted as a whole. The program was termed Emergency Maternity and Infant Care. The infant-care part of it was designed to take care of the sick in the first year of life and was not necessarily connected with the maternity part. But in conference with the Children's Bureau she was led to understand that most states included the infant care, and they had not refused to do so.

Dr. Mullins moved that recommendations of the Maternity and Infancy Committee be accepted. This motion was duly seconded and was carried.

Report of the Committee on the Control of Cancer

Last year this committee stated that the Executive Committee of the Women's Field Army would consider the advisability of using some of the money raised by the Women's Field Army for the encouragement of postgraduate study in cancer control, by offering any of the physicians associated with the New Hampshire cancer clinics an opportunity to take a refresher course. At a subsequent meeting of the committee it was voted to offer \$250 for a month's study in one of the centers where cancer is a major activity. Owing to war conditions the committee thought it advisable to offer the same type of assistance for a shorter period at a proportionate remuneration for two weeks or even one week. The chairman of the committee made arrangements with the Memorial Hospital and the Presbyterian Hospital in New York City and with three hospitals in Boston, whereby contacts could be made with the visiting staffs for clinical observation, surgery and x-ray and radium therapy.

Since January 1, four physicians connected with the New Hampshire clinics have taken advantage of this offer, and all have reported most satisfactory co-operation from these hospitals. More of the forty-five or more physicians associated with the clinics are urged to take advantage of this financial assistance to improve their knowledge of cancer diagnosis and treatment.

The usual three short letters from your committee have been sent to all the physicians in the State. The first one called attention to the importance of blood studies in the diagnosis and treatment of cancer, particularly in patients with tumors of lymph nodes in order to detect the possible presence of leukemia, and also stressed the importance of differentiating anemias from some types of cancer, particu-

larly cancer of the stomach. Attention was also called to the importance of blood studies with special reference to the indication for the need of transfusions in surgery of cancer patients, and in prolonged x-ray therapy. The second letter discussed the diagnostic significance of vaginal bleeding and of the differential diagnosis between carcinoma of the fundus and carcinoma of the cervix, with suggestions for procedures in making the clinical diagnosis. The third letter briefly discussed cancer of the lung with its symptoms, diagnosis and treatment, and emphasized the frequency of cough as an early symptom, the importance of an x-ray film in suggesting disease and the necessity of following this up with bronchoscopy. Copies of all our past letters have been requested by the Virginia Cancer Foundation for use in that state in their program of cancer education among the physicians.

The fourteen diagnostic clinics and treatment centers examined and treated about the same number of patients as in the previous year. Probably most of the patients who need to come for treatment have eventually arrived at one or another clinic, but it has been found that some of them have delayed coming on account of transportation difficulties, and also patients have not been able to return for checkups as frequently as they should for the same reason. It should be borne in mind that the Women's Field Army will, on application, provide some method of transportation for these people.

The Women's Field Army is also distributing the usual number of educational pamphlets, especially during the month of April, which has been designated Cancer Control Month by the Congress of the United States. They also have furnished many indigent patients with cancer dressings that are made up from linen and cotton collected from the public.

The American Society for the Control of Cancer is sponsoring cancer education in secondary schools in a large number of states throughout the country. In co-operation with educational authorities, some type of cancer instruction has been introduced into many high schools and junior high schools. It has been found that not only are young people interested, but their knowledge of cancer as it is taught in the schools, based primarily on courses in biology, is of definite benefit in instructing the older people in their families. It has been found that both students and teachers are interested in this activity, and here in New Hampshire we have found much interest and a definitely favorable response from the showing of cancer films in the high schools.

Your committee would like an expression of approval of cancer education in the secondary schools of this state before it is taken up as a state-wide project with a larger group of school administrators. We also request continued co-operation on the part of all physicians in the State in responding to requests for physical examinations. This is one phase of the work of the Women's Field Army that is stressed constantly in their literature and in the contacts of the workers with other women.

Your committee has spent \$43.40 on printing, stationery and postage. The balance of our \$50 appropriation has been returned to the treasurer. We respectfully request an appropriation of \$50 for the coming year.

GEORGE C. WILKINS, *Chairman*
RALPH E. MILLER
GEORGE F. DWINELL, *Secretary*

Dr. Mullins suggested that the appropriation of \$50 be continued and moved the adoption of this portion of the report of the Committee on Officers' Reports. This motion was duly seconded and carried.

Report of the Committee on Medical Education and Hospitals

The activities of this committee have been necessarily limited. This is due in the first place to the fact that there have been no fellowships offered by the Commonwealth Fund under present war conditions, presumably because there would be so few men with either the age eligibility requirements or the available time.

The committee has collaborated with various regional and national agencies and committees in surveys pertaining to postwar training opportunities that might be available or might be established in the State or the New England area.

The Speakers' Bureau has been used by a few county societies, and this activity is being continued so far as there is a demand.

The only positive activity of the chairman has been the appointment to membership on the Regional Committee of the Wartime Graduate Medical Program. Region No. 1 consists of Maine, New Hampshire, Vermont and Massachusetts. This committee has been actively engaged in the arrangements of programs at the various military stations in the region. These programs have been organized as a result of a survey of the various commanding officers to line up the topics that seem most desirable to them. These meetings have been held at frequent intervals, and once each month a bulletin announcing all meetings is issued. The speakers for these programs have been obtained by this committee. These meetings have been primarily for the men in military service within the district of the meeting, but they have also been open to civilian physicians. It is probable that this program will be continued indefinitely.

JOHN P. BOWLER, Chairman
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr. Mullins moved the adoption of this report. This motion was duly seconded and was carried.

Report of the Committee on Medical Preparedness

The only activity of this committee has been to assist in the relocation of physicians to care for the civilian needs. In two cities attempts have been made to work out plans so that one doctor will be on duty each night. The doctors will take turns in this work, so that the others may secure more sleep.

DEERING G. SMITH, Chairman
Ezra A. Jones
CARLETON R. METCALF

Dr. Mullins moved the adoption of this report. This motion was duly seconded and was carried.

Report of the Committee on Mental and Social Hygiene

New Hampshire has more agencies and, when filled, a larger number on the staff of these agencies in the performance of social and mental hygiene than ever before. The blind and partially blind, the hard of hearing and the deaf all receive attention. The crippled children, the shut-in and the handicapped adults receive attention from a variety of agencies, and some of the activity on their behalf is from voluntary contributions. Through the efforts of our governor, state employees and inmates of state institutions are having x-ray films of the chest for the detection and treatment of tuberculosis.

There are other fields of human misery less well covered. Our state has many intelligent sufferers from chronic arthritis who are poor and unaided. Many of our general hospitals could be relieved of patients much more expeditiously if there were available in the State a number of good and not too expensive convalescent homes. Institutions are not desirable if they can be avoided, but we must depend on other states for the instruction of our blind and deaf, and we have no institution for the care and treatment of patients suffering from epilepsy, of whom there are a large number in our other institutions.

The absorption of the young men and women of the State by war emphasizes to the trained observer the frequency

in the remaining population not only of senile persons but of psychopathic personalities. We know that the number of senile persons in proportion to the population has increased, and it is probable that pathologic personalities are also on the increase. These persons are neither fully insane, feeble-minded or epileptic, but nevertheless they are not normal and it is unfortunate that they receive no recognition but with those with senile dementias are committed to the State Hospital and burden the space intended for the acutely insane.

We have many special agents, but there are very few psychiatric social workers in the State. We are seriously wanting in psychologists, and in our rural districts there are many psychotic persons who with their families would be greatly benefited by a little special psychiatric advice.

To use the numerous mental tests for the diagnosis of mental deficiency and derangements there should be several psychologists available to the school departments, and in the near future some competent analyzers of human aptitudes are needed to aid in the educational field and rehabilitation. An amount of this work, relatively small in comparison with the needs, has been furnished by the colleges, by the Laconia State School and principally by the State Hospital. The performance of this work calls for support from some source, and it may be properly questioned whether or not state institutions and colleges should be the source of this support, or whether clinics should be publicly maintained.

The sensible publicity approach to venereal disease has been highly advantageous, and we believe that its treatment is much more general and effective than it was some years ago. So far as we can learn, the law requiring blood examination before marriage is properly complied with and fairly efficiently. The law permitting sterilization of the insane, feeble minded and epileptic in institutions is operating conservatively, and we hope in conformity with the letter of the law, which permits operation in hereditary and transmissible cases.

Unknown to many, the State has a law that was intended to limit the marriage of defective persons and is found in Chapter 286 on page 1164 of Volume II of the Public Laws of 1926. As near as we can learn, this law is practically ignored. A few clerks have refused licenses and referred the parties to the State Board of Health for an examination. Under this law it is the duty of all superintendents of schools and all having charge of instruction in private schools and state institutions to report the names of all defectives discharged through those sources. The intention of the law is that the names of those persons be kept on file in the Bureau of Vital Statistics and be available there not only for reference by city clerks but as accumulating data on the number of such persons in the State and for the detection of hereditary families. It is not evident that this part of the law is complied with. There are now 700 inmates at Laconia State School and this is probably not more than 12 per cent of the mentally deficient in the State. We have compiled for years vital statistics, but no one knows how many mentally deficient there are in New Hampshire.

B. W. BAKER, Chairman
CHARLES H. DOLLOFF
JOHN B. McKENNA

Dr. Mullins for the Committee on Officers' Reports agreed that there is a need for more specialized workers in mental and social hygiene in this state, and that proper presentations should be made through the appropriate channels to the State Legislative Assembly in 1945. He moved the adoption of this portion of the Report of the Committee on Officers' Reports. The motion was duly seconded and was carried.

Report of the Committee on Public Health

This, the third year of this committee, has been uneventful. In spite of the increase in activity in industrial fields throughout New England, we of New Hampshire have experienced proportionately a very small increase in man-

r along industrial lines, and this is particularly true e eliminates the Portsmouth area, where so many citi- have been employed in the Portsmouth Navy Yard, her with the lumber centers in the northern section of state. For this reason, the industrial public-health tion in New Hampshire has presented a very minor lem as compared with that in some of the more active rs of manufacture in other sections of the country. e housing situation in and around Portsmouth has ed some anxiety, but this has been greatly relieved by daily transportation of employees to and from their work. : a result of the previous programs of the Committee ublic Health, we feel that the groundwork of this com- ee is well established. We believe that the health of trial employees in this state ranks high and that the dards under which the employees work and live are ng the best. This is substantiated to a large degree by minimum number of absentee records among the em- ees, and this takes into consideration the fact that some e employees travel many miles a day to and from their e of employment and also that the average age of em- ees has increased owing to the drafting of the younger

our committee has had no reference from either em- ers, employees or other sources during the entire year, this again speaks well for our working conditions and th standards, and accounts for the inaction of this mittee.

e have received regular communications in connection i industrial hygiene as published by the United States lic Health Service, together with outlines of programs a various industrial centers.

Unfortunately, your chairman was unable to attend the h Annual Congress on Industrial Health, which was held Chicago in February of this year, owing to the uncer- tity of family affairs at that time, and as yet we have not ived the proceedings of this meeting, so consequently unable to give you the particulars at this writing.

n submitting this report, may we state that it has been a sure to serve on the Committee on Public Health of the e Hampshire Medical Society and, although the duties e been somewhat limited, we feel certain that there will more and more problems presented to this committee time goes on.

HARRIS E. POWERS, *Chairman*
ANTHONY E. PETERS
CLINTON R. MELLIN

Dr. Mullins said that the Committee on Officers' ports was pleased to note the high standard of ublic health in New Hampshire. The fact that complaints have been voiced was a good in- ation that conditions were satisfactory. He ved the adoption of this report. This motion is duly seconded and was carried.

Report of the Committee on Tuberculosis

It is with deep regret that the Committee on Tuberculosis rds in this report the death on March 30, 1944, of one of members, Dr. Clarence O. Coburn, of Manchester. r thirty-eight years Dr. Coburn had been engaged in the ivate practice of medicine in his native city. He had ded his practice to internal medicine, in which field he was dely recognized for his unusual skill, judgment and re- urcefulness. A tried and true physician, Dr. Coburn was all times one who exemplified the finest ideals in citizen- ip and service to his fellow men. During the years 1919 to 21 he was president of the New Hampshire Tuberculosis ssociation. His active interest and support in the campaign ainst the disease was maintained until the end. His death a sad and severe loss to this Society and particularly to the ommittee on Tuberculosis.

As has been stated in previous reports, the encouraging gress that has been made in combating tuberculosis in ew Hampshire is due largely to the efforts of the members e New Hampshire Medical Society. The physicians of ew Hampshire are the first line of defense and attack in e fight against the disease. They are the "case finders" par

excellence in the program of early diagnosis, particularly of open cases, in which prompt supervision and treatment are of utmost importance.

During the past year a larger number of possible tuber- culous patients than for some years past have been referred to the chest diagnostic clinics maintained throughout the State. It is felt that these clinics perform their greatest service when they assist the members of the New Hampshire Medical Society in the diagnosis of tuberculosis among their patients who present suspicious signs and symptoms.

An excellent piece of tuberculosis case finding continues to be carried on at the Selective Service induction center in Manchester. An essential part of the exacting examinations at this induction center is an x-ray examination of the chest for every man. All men found to have roentgenographic evidence of tuberculosis are afforded prompt follow-up. In this way, the Selective Service Boards are not only keeping tuberculosis out of the military forces but are also providing a splendid case-finding program for a sizable segment of the population of our state.

Since June, 1943, the chests of approximately 4500 workers in the industries of this state have been examined roentgeno- graphically. This has been accomplished through a joint program inaugurated and maintained by the Industrial Hygiene Division of the State Department of Health and the New Hampshire Tuberculosis Association. The remarkable success of this program is due to the whole-hearted co- operation of management and labor, including industrial physicians and labor organizations. This program is resulting in the discovery of large numbers of potentially active cases of tuberculosis. The program is progressing rapidly.

For some years your committee has emphasized the great value of the chest roentgenogram in the discovery of tuber- culous patients. It is well known that tuberculous lesions can be seen in the chest roentgenographically before signs can be heard with the stethoscope. We again urge the mem- bers of the New Hampshire Medical Society to use the roentgenographic method frequently when examining chests. The New Hampshire Tuberculosis Association is ready to provide chest x-ray films for persons referred by physicians when these persons are unable to pay for them. Furthermore, the New Hampshire State Sanatorium and the New Hamp- shire Tuberculosis Association continue to offer their services in the interpretation of chest x-ray films sent to them for diagnosis.

We also urge prompt examination of all members of the family when a case of tuberculosis is found, since in a house- hold where an open case has been discovered we usually find that all members are positive tuberculin reactors.

We also urge at least a tuberculin test for all persons car- ing for children. This should be a routine procedure for nursemaids, governesses and others in contact with children.

In the treatment of tuberculosis, bed rest continues to be emphasized. It is generally considered that a bed-rest regime is extremely helpful in deciding on the clinical activity of the disease. Surgical procedures such as pneumothorax phreni- cotomy, phrenicotomy and thoracoplasty are still employed in properly selected cases as aids to the cure of the disease.

Beginning July 1, 1943, the appropriation for hospitaliza- tion of tuberculosis cases under the advanced case appropria- tion was transferred from the State Department of Public Welfare to the State Department of Health. Applications for admission of patients to the Pembroke Sanatorium are now sent to the State Department of Health. The medical supervision of the patients at the Pembroke Sanatorium is therefore under the jurisdiction of the State Department of Health.

Dr. Rufus R. Little, superintendent and medical director of the New Hampshire State Sanatorium at Glenciff, has been appointed consultant on tuberculosis to the State Department of Health. This program has proved extremely helpful, and the work of the two sanatoriums is now splen- didly co-ordinated. Dr. Little visits the Pembroke Sanato- rium once a week. Once in three weeks, chest surgery is per- formed at the Glenciff Sanatorium for patients from both institutions. These operations comprise thoracoplasty, lobectomy, phrenicectomy and so forth. Pneumothorax is a routine procedure at both sanatoriums.

Our nation is now in the final stages of the second great war. It appears that up to the present time there has been no in- crease in the number of deaths or the death rate from tuber- culosis in New Hampshire. The number of *known* cases has

Report of the Committee on Medical Education and Hospitals

The activities of this committee have been necessarily limited. This is due in the first place to the fact that there have been no fellowships offered by the Commonwealth Fund under present war conditions, presumably because there would be so few men with either the age eligibility requirements or the available time.

The committee has collaborated with various regional and national agencies and committees in surveys pertaining to postwar training opportunities that might be available or might be established in the State or the New England area.

The Speakers' Bureau has been used by a few county societies, and this activity is being continued so far as there is a demand.

The only positive activity of the chairman has been the appointment to membership on the Regional Committee of the Wartime Graduate Medical Program. Region No. 1 consists of Maine, New Hampshire, Vermont and Massachusetts. This committee has been actively engaged in the arrangements of programs at the various military stations in the region. These programs have been organized as a result of a survey of the various commanding officers to line up the topics that seem most desirable to them. These meetings have been held at frequent intervals, and once each month a bulletin announcing all meetings is issued. The speakers for these programs have been obtained by this committee. These meetings have been primarily for the men in military service within the district of the meeting, but they have also been open to civilian physicians. It is probable that this program will be continued indefinitely.

JOHN P. BOWLER, *Chairman*
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr. Mullins moved the adoption of this report. This motion was duly seconded and was carried.

Report of the Committee on Medical Preparedness

The only activity of this committee has been to assist in the relocation of physicians to care for the civilian needs. In two cities attempts have been made to work out plans so that one doctor will be on duty each night. The doctors will take turns in this work, so that the others may secure more sleep.

DEERING G. SMITH, *Chairman*
EZRA A. JONES
CARLETON R. METCALF

Dr. Mullins moved the adoption of this report. This motion was duly seconded and was carried.

Report of the Committee on Mental and Social Hygiene

New Hampshire has more agencies and, when filled, a larger number on the staff of these agencies in the performance of social and mental hygiene than ever before. The blind and partially blind, the hard of hearing and the deaf all receive attention. The crippled children, the shut-in and the handicapped adults receive attention from a variety of agencies, and some of the activity on their behalf is from voluntary contributions. Through the efforts of our governor, state employees and inmates of state institutions are having x-ray films of the chest for the detection and treatment of tuberculosis.

There are other fields of human misery less well covered. Our state has many intelligent sufferers from chronic arthritis who are poor and unaided. Many of our general hospitals could be relieved of patients much more expeditiously if there were available in the State a number of good and not too expensive convalescent homes. Institutions are not desirable if they can be avoided, but we must depend on other states for the instruction of our blind and deaf, and we have no institution for the care and treatment of patients suffering from epilepsy, of whom there are a large number in our other institutions.

The absorption of the young men and women of the State by war emphasizes to the trained observer the frequency

in the remaining population not only of senile persons but of psychopathic personalities. We know that the number of senile persons in proportion to the population has increased, and it is probable that pathologic personalities are also on the increase. These persons are neither fully insane, feeble-minded or epileptic, but nevertheless they are not normal and it is unfortunate that they receive no recognition but with those with senile dementias are committed to the State Hospital and burden the space intended for the acutely insane.

We have many special agents, but there are very few psychiatric social workers in the State. We are seriously wanting in psychologists, and in our rural districts there are many psychotic persons who with their families would be greatly benefited by a little special psychiatric advice.

To use the numerous mental tests for the diagnosis of mental deficiency and derangements there should be several psychologists available to the school departments, and in the near future some competent analyzers of human aptitudes are needed to aid in the educational field and rehabilitation. An amount of this work, relatively small in comparison with the needs, has been furnished by the colleges, by the Laconia State School and principally by the State Hospital. The performance of this work calls for support from some source, and it may be properly questioned whether or not state institutions and colleges should be the source of this support, or whether clinics should be publicly maintained.

The sensible publicity approach to venereal disease has been highly advantageous, and we believe that its treatment is much more general and effective than it was some years ago. So far as we can learn, the law requiring blood examination before marriage is properly complied with and fairly efficiently. The law permitting sterilization of the insane, feeble minded and epileptic in institutions is operating conservatively, and we hope in conformity with the letter of the law, which permits operation in hereditary and transmissible cases.

Unknown to many, the State has a law that was intended to limit the marriage of defective persons and is found in Chapter 286 on page 1164 of Volume II of the Public Laws of 1926. As near as we can learn, this law is practically ignored. A few clerks have refused licenses and referred the parties to the State Board of Health for an examination. Under this law it is the duty of all superintendents of schools and all having charge of instruction in private schools and state institutions to report the names of all defectives discharged through those sources. The intention of the law is that the names of those persons be kept on file in the Bureau of Vital Statistics and be available there not only for reference by city clerks but as accumulating data on the number of such persons in the State and for the detection of hereditary families. It is not evident that this part of the law is complied with. There are now 700 inmates at Laconia State School and this is probably not more than 12 per cent of the mentally deficient in the State. We have compiled for years vital statistics, but no one knows how many mentally deficient there are in New Hampshire.

B. W. BAKER, *Chairman*
CHARLES H. DOLLOFF
JOHN B. MCKENNA

Dr. Mullins for the Committee on Officers' Reports agreed that there is a need for more specialized workers in mental and social hygiene in this state, and that proper presentations should be made through the appropriate channels to the State Legislative Assembly in 1945. He moved the adoption of this portion of the Report of the Committee on Officers' Reports. The motion was duly seconded and was carried.

Report of the Committee on Public Health

This, the third year of this committee, has been uneventful. In spite of the increase in activity in industrial fields throughout New England, we of New Hampshire have experienced proportionately a very small increase in man-

power along industrial lines, and this is particularly true in the Portsmouth area, where so many citizens have been employed in the Portsmouth Navy Yard, together with the lumber centers in the northern section of our state. For this reason, the industrial public-health situation in New Hampshire has presented a very minor problem as compared with that in some of the more active centers of manufacture in other sections of the country.

The housing situation in and around Portsmouth has caused some anxiety, but this has been greatly relieved by the daily transportation of employees to and from their work.

As a result of the previous programs of the Committee on Public Health, we feel that the groundwork of this committee is well established. We believe that the health of industrial employees in this state ranks high and that the standards under which the employees work and live are among the best. This is substantiated to a large degree by the minimum number of absentee records among the employees, and this takes into consideration the fact that some of the employees travel many miles a day to and from their place of employment and also that the average age of employees has increased owing to the drafting of the younger men.

Your committee has had no reference from either employers, employees or other sources during the entire year, and this again speaks well for our working conditions and health standards, and accounts for the inaction of this committee.

We have received regular communications in connection with industrial hygiene as published by the United States Public Health Service, together with outlines of programs from various industrial centers.

Unfortunately, your chairman was unable to attend the Sixth Annual Congress on Industrial Health, which was held in Chicago in February of this year, owing to the uncertainty of family affairs at that time, and as yet we have not received the proceedings of this meeting, so consequently are unable to give you the particulars at this writing.

In submitting this report, may we state that it has been a pleasure to serve on the Committee on Public Health of the New Hampshire Medical Society and, although the duties have been somewhat limited, we feel certain that there will be more and more problems presented to this committee as time goes on.

HARRIS E. POWERS, *Chairman*
ANTHONY E. PETERS
CLINTON R. MELLIN

Dr. Mullins said that the Committee on Officers' Reports was pleased to note the high standard of public health in New Hampshire. The fact that no complaints have been voiced was a good indication that conditions were satisfactory. He moved the adoption of this report. This motion was duly seconded and was carried.

Report of the Committee on Tuberculosis

It is with deep regret that the Committee on Tuberculosis records in this report the death on March 30, 1944, of one of its members, Dr. Clarence O. Coburn, of Manchester. For thirty-eight years Dr. Coburn had been engaged in the private practice of medicine in his native city. He had devoted his practice to internal medicine, in which field he was widely recognized for his unusual skill, judgment and resourcefulness. A tried and true physician, Dr. Coburn was at all times one who exemplified the finest ideals in citizenship and service to his fellow men. During the years 1919 to 1921 he was president of the New Hampshire Tuberculosis Association. His active interest and support in the campaign against the disease was maintained until the end. His death is a sad and severe loss to this Society and particularly to the Committee on Tuberculosis.

As has been stated in previous reports, the encouraging progress that has been made in combating tuberculosis in New Hampshire is due largely to the efforts of the members of the New Hampshire Medical Society. The physicians of New Hampshire are the first line of defense and attack in the fight against the disease. They are the "case finders" par

excellence in the program of early diagnosis, particularly of open cases, in which prompt supervision and treatment are of utmost importance.

During the past year a larger number of possible tuberculous patients than for some years past have been referred to the chest diagnostic clinics maintained throughout the State. It is felt that these clinics perform their greatest service when they assist the members of the New Hampshire Medical Society in the diagnosis of tuberculosis among their patients who present suspicious signs and symptoms.

An excellent piece of tuberculosis case finding continues to be carried on at the Selective Service induction center in Manchester. An essential part of the exacting examinations at this induction center is an x-ray examination of the chest for every man. All men found to have roentgenographic evidence of tuberculosis are afforded prompt follow-up. In this way, the Selective Service Boards are not only keeping tuberculosis out of the military forces but are also providing a splendid case-finding program for a sizable segment of the population of our state.

Since June, 1943, the chests of approximately 4500 workers in the industries of this state have been examined roentgenographically. This has been accomplished through a joint program inaugurated and maintained by the Industrial Hygiene Division of the State Department of Health and the New Hampshire Tuberculosis Association. The remarkable success of this program is due to the whole-hearted cooperation of management and labor, including industrial physicians and labor organizations. This program is resulting in the discovery of large numbers of potentially active cases of tuberculosis. The program is progressing rapidly.

For some years your committee has emphasized the great value of the chest roentgenogram in the discovery of tuberculous patients. It is well known that tuberculous lesions can be seen in the chest roentgenographically before signs can be heard with the stethoscope. We again urge the members of the New Hampshire Medical Society to use the roentgenographic method frequently when examining chests. The New Hampshire Tuberculosis Association is ready to provide chest x-ray films for persons referred by physicians when these persons are unable to pay for them. Furthermore, the New Hampshire State Sanatorium and the New Hampshire Tuberculosis Association continue to offer their services in the interpretation of chest x-ray films sent to them for diagnosis.

We also urge prompt examination of all members of the family when a case of tuberculosis is found, since in a household where an open case has been discovered we usually find that all members are positive tuberculin reactors.

We also urge at least a tuberculin test for all persons caring for children. This should be a routine procedure for nursemaids, governesses and others in contact with children.

In the treatment of tuberculosis, bed rest continues to be emphasized. It is generally considered that a bed-rest regime is extremely helpful in deciding on the clinical activity of the disease. Surgical procedures such as pneumothorax phrenicotomy, phrenicotomy and thoracoplasty are still employed in properly selected cases as aids to the cure of the disease.

Beginning July 1, 1943, the appropriation for hospitalization of tuberculosis cases under the advanced case appropriation was transferred from the State Department of Public Welfare to the State Department of Health. Applications for admission of patients to the Pembroke Sanatorium are now sent to the State Department of Health. The medical supervision of the patients at the Pembroke Sanatorium is therefore under the jurisdiction of the State Department of Health.

Dr. Rufus R. Little, superintendent and medical director of the New Hampshire State Sanatorium at Glencliff, has been appointed consultant on tuberculosis to the State Department of Health. This program has proved extremely helpful, and the work of the two sanatoriums is now splendidly co-ordinated. Dr. Little visits the Pembroke Sanatorium once a week. Once in three weeks, chest surgery is performed at the Glencliff Sanatorium for patients from both institutions. These operations comprise thoracoplasty, lobectomy, phrenicectomy and so forth. Pneumothorax is a routine procedure at both sanatoriums.

Our nation is now in the final stages of the second great war. It appears that up to the present time there has been no increase in the number of deaths or the death rate from tuberculosis in New Hampshire. The number of *known* cases has

increased, but not the *known active*—so-called “open”—cases of tuberculosis. Because of the careful x-ray chest surveys at the Induction Center by the War Department, and among workers in industry by the State Department of Health and the New Hampshire Tuberculosis Association, a definite increase in known tuberculosis cases has been recorded. Although these cases are mostly in the arrested stage, they nevertheless constitute a potentially active source of the disease. The necessity for proper medical advice and supervision in such cases is obvious.

The fact remains that tuberculosis and war are still allies. Infection with tubercle bacilli is still widespread among the people. Tuberculin-test surveys indicate that approximately 50 per cent of the adult population of our state harbor tubercle bacilli. The infection is held in abeyance in many cases because of adequate physical resistance on the part of those who are infected. Longer hours of labor and increased mental and physical strain tend to lower physical resistance, thereby predisposing toward the breakdown of a previously quiescent or so-called “healed” lesion. To use the layman’s words, tired bodies may permit the ever-lurking tuberculosis germs to attack the lung cells successfully.

There must be no relaxation in the fight against the tubercle bacillus. In fact, the fight must be carried on with ever greater aggressiveness to hold the gains won.

Your committee avails itself of this opportunity to express its deep sense of gratitude and appreciation for the wholehearted assistance and encouragement accorded to it by the members of the New Hampshire Medical Society.

ROBERT B. KERR, *Chairman*
RICHARD C. BATT

Dr. Mullins for the Committee on Officers’ Reports congratulated the Committee on Tuberculosis on its excellent and inclusive report. The change of administration from the Department of Public Welfare to that of Public Health seemed to him a proper step. The suggestion of more frequent use of the x-ray in suspected cases of tuberculosis was particularly commended. Dr. Mullins moved the adoption of this report, and the motion was duly seconded and was carried.

Report of the Delegate to the House of Delegates of the American Medical Association

The annual session of the American Medical Association was held at Chicago, June 7, 8 and 9, 1943, and was limited to meetings of the House of Delegates and to two general meetings. Your delegate served as chairman of the Reference Committee on Reports of Officers. He has endeavored to select the high points of the meeting for this report to the New Hampshire Medical Society.

Elliott P. Joslin, of Boston, was given the Distinguished Service Award and Herman I. Kretschmer, of Chicago, was chosen president-elect.

The Committee on Planning of Postwar Medical Services was established, to co-operate and collaborate with other agencies concerned with these problems.

The Board of Trustees made a lengthy report dealing with hospital corporations engaging in the practice of medicine. That the Blue Cross plans to give medical service with or without the approval of the medical profession there can be no doubt after reading this report. It was voted that hospitals should not be permitted to practice medicine, and the House reiterated its disapproval of the injecting of a third party into the personal relation of the patient and the physician. It further voted “that the practice of radiology, pathology and anesthesiology is the practice of medicine just as much as is the practice of surgery or internal medicine, and that it is only a short step from including the first three in a medical-service plan to including the whole field of medicine in such a plan.”

The Council on Medical Service and Public Relations was established. The functions of this council are as follows: to make available facts, data and medical opinions with respect to timely and adequate rendition of medical care to

the American people; to inform constituent associations and component societies of proposed changes affecting medical care in the nation; to inform constituent associations and component societies regarding the activities of the council; to investigate matters pertaining to the economic, social and similar aspects of medical care for all the people; to study and suggest means for the distribution of medical service to the public consistent with the principles adopted by the House of Delegates; to develop and assist committees on medical service and public relations originating within the constituent associations and component societies of the American Medical Association.

The action of the federal government in making funds available for maternity and infant care for the wives and infants of enlisted men was approved, and adoption was urged of a plan under which the federal government would provide for the wives of enlisted men a stated allotment for medical, hospital, maternity and infant care similar to the allotments already provided for the maintenance of dependents, leaving the actual arrangements with respect to fees to be fixed by mutual agreement with the wife and the physician of her choice. This action was similar to that taken by the New Hampshire House of Delegates last May. A copy of the resolution urging that the method of making available these funds be changed to an allotment basis was sent to each congressman and each senator. (After considerable discussion in the House of Representatives, the proposal was rejected by a vote of 115 to 8.)

The Board of Trustees, in its report devoted considerable space to the subject of prepaid medical service. It gave the history of the various plans and discussed the progress that had been made under them. This report was published in the April 24, 1943, issue of the *Journal of the American Medical Association*. In view of the present discussion of a prepayment medical plan in our state, it seems advisable to point out some of the dangers and complications of such a plan. These were first included in a special report, approved by the House of Delegates in 1935, and seem no less applicable today than at that time; they are as follows:

The adoption and operation of a medical plan where it is unnecessary.

The stimulus aroused by good plans among irresponsible organizers to develop and operate imitations and counterfeits.

The establishment in medical practice of dangerous patterns, following the adoption of undesirable types of plans.

The compromise of medical societies in the corporate practice of medicine or in the operation of insurance companies as a result of an insufficient study of state statutes and case law.

Failure, in the operation of a plan, to conform to the *Principles of Medical Ethics*.

The almost inevitable transition of voluntary insurance plans into compulsory contributory sickness insurance systems operated by the state.

The difficulties involved in the failure adequately to provide for complete control of medical affairs by the medical profession.

The “freezing” of medical fees at a point below that which is consistent with good medical care.

Failure to bear constantly in mind that a medical society plan is an experiment in the methods of distributing medical service and that it may have only a temporary usefulness, may need frequent or drastic modifications or may need to be discarded entirely.

Medical society plans must not be considered or accepted as a substitute for the regular practice of medicine as applied to the majority of people. If it is believed such plans may be useful, they should be considered merely as supplementary facilities in the distribution of medical service. They should be used only so long and in such a manner as they serve efficiently to make more easily available to low-income groups a high quality of medical care.

The April 29, 1944, issue of the *Journal of the American Medical Association* contains the report of the Board of Trustees for the past year. It is stated there: “The population group that has incomes too small to meet health necessities in the way of food, clothing, fuel and shelter cannot be expected to budget or make prepayments for catastrophic

These 'medically indigent' are always more of an economic than of a medical problem, since their medical care, regardless of the manner by which the cost is met, must, as always, be paid for directly or indirectly out of higher incomes." The necessary legislation has been secured and administrative organizations for the operation of prepayment plans are functioning in 14 states, and some part of the program has been undertaken in ten additional states. These plans have been in operation from a few months to seven years, but the demand for the service is apparently slight, with the exception of Michigan a very small proportion of the population is enrolled. The figures given are as of 1933, in most instances the latter part of the year: California, 88,000; Colorado, 5,000; Massachusetts, 23,000; Michigan, 600,455; Missouri and Kansas, 6,500; New Jersey, 100,000; New York, 17,000 (with 22,000 in a second plan, and 30,000 in a third plan); North Carolina, 13,031; Pennsylvania, 10,000; and Texas, 378. It is evident that prepayment medical plans are still in the experimental stage, and it seems as if the

New Hampshire Medical Society should consider further the advisability of launching its plan at this time.

DEERING G. SMITH

Dr. Mullins for the Committee on Officers' Reports expressed indebtedness to Dr. Smith for a thought-provoking summary of the actions of the American Medical Association. He added that consideration of these facts should guide the Society in its decisions regarding the various programs being instituted by the federal government. He moved the adoption of this report. This motion was duly seconded and was carried.

(To be concluded)

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30391

PRESENTATION OF CASE

A fifty-nine-year-old engineering executive was seen at home because of difficulty in breathing. The patient had always been active. While in college he had a tendency to have rapid or irregular heart action, which occasioned interest but did not bother him. At the age of forty, however, after a sleep, he was seized by his first attack of palpitation. The heart action was forceful and rapid, and the attack lasted for half an hour after dinner. Since then he had had a great deal of palpitation, mostly jumps or skips but occasionally spells of heart racing (usually regular). The palpitation was especially apparent when he was tired and at rest. Examination of the heart during these attacks showed extrasystoles. The blood pressure was 135 systolic, 80 diastolic. An electrocardiogram at the age of forty-eight showed a normal rhythm with a rate of 92. The PR interval was 0.20 second, the RS interval 0.06 second, and the T waves upright in all leads; the axis was normal. The following year he had an attack of ureteral colic on the right. The heart sounds at that time were poor. There was a definite third sound, as well as gallop rhythm, which was marked in the upright position. The blood

*On leave of absence.

pressure was 150 systolic, 100 diastolic. An electrocardiogram a year later showed a normal rhythm with a rate of 100, a PR interval of 0.24 second, slight left-axis deviation and frequent premature ventricular beats. These findings persisted for the next two years. There was no pain at any time. Two years later a slight presystolic gallop rhythm was heard at the apex. Frequent premature beats were present. The blood pressure was 160 systolic, 100 diastolic. At another examination he had a bigeminal pulse. The heart rhythm was definitely coupled with an extrasystole every other beat. The blood pressure was 150 systolic, 85 diastolic. An electrocardiogram showed normal sinus rhythm, a rate of 94, a PR interval of 0.24 second and a QRS interval of 0.08 second. T₁ and T₂ were low, and T₃ upright. There was slight shift of the axis to the right. Ventricular extrasystoles were present throughout the record, giving it a bigeminal rhythm. He was given potassium iodide for two or three months, with rest, and felt much better. The heart was regular and rapid. When fifty-five years old he had lobar pneumonia. He was hospitalized for three weeks, and during this illness "his heart did beautifully." A gallop rhythm or third sound persisted. The blood pressure was 120 systolic, 80 diastolic. Six months later he experienced irregularity of the heart beat associated with a desire to take a deep breath. He was given 0.2 gm. of quinidine twice a day for ten days, with definite benefit, but he was then hospitalized.

Examination on admission showed slight cyanosis. The left border of cardiac dullness was 14 cm. to the left of the midline. The heart was rapid but regular. The sounds were of poor quality. There was pulsus alternans, with a marked protodiastolic gallop at the apex. The pulmonic second sound was greater than the aortic. There were wheezes throughout both lung fields, with medium moist rales at the right base. The blood pressure was 145 systolic, 95 diastolic. The blood counts were normal. The

basal metabolic rate was normal. An electrocardiogram revealed ventricular premature beats interrupting sinoauricular tachycardia at a rate of 115. There was slight auriculoventricular block, with a PR interval of 0.22 second. The QRS waves

cardiogram (Fig. 1) showed a PR interval of 0.3 second, a rate of 90, slight inversion of T_1 , T_2 and T_4 , and slurred QRS complexes in Leads 1, 2 and 3; there was an increase in voltage over the previous records. His condition steadily improved until the

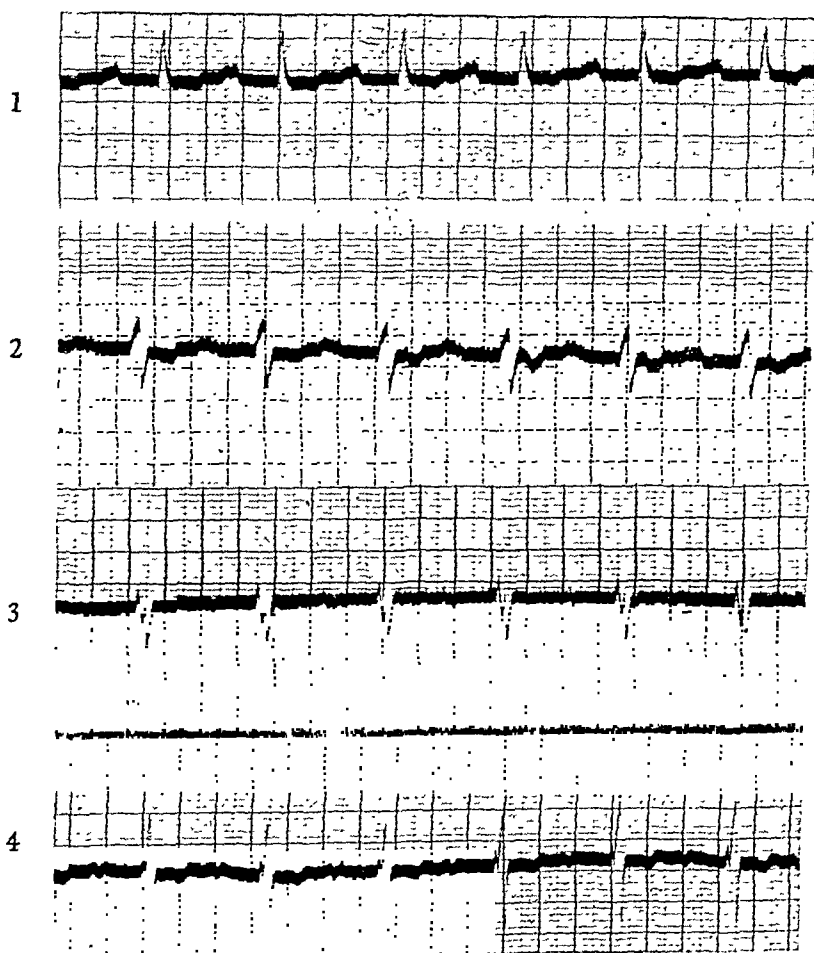


FIGURE 1.

were of low voltage, slurred and slightly widened. The T waves were low in all four leads.

The patient was given aminophyllin and sedatives as desired. After two weeks of bed rest he showed a rising pulse rate (130), persistent rales in both lungs and, *except when taking aminophyllin*, Cheyne-Stokes respirations. He was given 0.4 gm. of digitalis for four days and then 0.03 gm. daily. At the end of that period he woke up early one morning with a dull ache in the right groin which extended down to the knee and lasted for several hours. The leg seemed to buckle under him. Examination of the leg was negative. An electro-

twenty-eighth hospital day, when, on moving, he suddenly had a sharp, stabbing, fleeting, nonradiating pain in the left anterior chest without interference to breathing. On questioning, he stated that he had experienced a similar pain in the right chest the previous night. Examination was negative except for a presystolic and a protodiastolic gallop. The heart sounds were of very poor quality; the second sound was almost inaudible. The blood pressure was 135 systolic, 90 diastolic. In the next ten days his condition improved considerably. the gallop rhythm became hardly noticeable,

he was discharged on the forty-sixth hospital

the course of the next three and a half years it well, although he became fatigued rather and was conscious of the irregularities of heart beat and breathing. On such occasions a p rhythm was present. At all other times, the i was rapid but regular, the sounds were of quality, and there were no murmurs. Distended veins were occasionally seen. During most of period he received digitalis, phenobarbital and butal.

Following a severe upper respiratory infection which he slowly recovered, he developed pneumonia and Cheyne-Stokes breathing at night. There was pulsus alternans, and the heart rate was 115. The blood pressure was 115 systolic, 80 diastolic. He was further digitalized. Nocturnal pneumonia and Cheyne-Stokes breathing disappeared about two weeks. The pulsus alternans could not be heard, but there were four definite sounds in the heart. The pulse, however, remained high. He continued to take 0.03 gm. of digitalis daily. It was decided that he should retire from his business.

The next month, following the emotional strain of selling his home and closing his business, he again developed nocturnal Cheyne-Stokes breathing. Examination showed slight dyspnea. The pulse was normal at 108. The blood pressure was 150 systolic, 100 diastolic, with evidence of pulsus alternans. Both arterial and venous pulsations were slightly increased in the neck. The cardiac impulse was felt 4 cm. to the left of the midsternal line in the sixth intercostal space. Marked diastolic gallop rhythm was present. A slight apical systolic murmur was heard. The pulmonic second sound was increased. The lungs were clear except for persistent fine rales at both bases. The liver was palpable two finger-breadths below the costal margin but was not tender. There was no edema. The patient was given 1 cc. of Salyrgan, and the fluid intake was limited to 1200 cc. There was good diuresis. Cheyne-Stokes breathing continued, however, and one week later basal rales were again heard. He was given 1 cc. of Salyrgan and theophyllin intravenously every fourth day, and 0.2 gm. of aminophyllin after each meal. He improved considerably during the next ten days. The following morning he awoke and was unable to speak clearly, to feed himself or to recognize simple objects, such as a fork and a spoon, or what to do with them. He was, however, conscious of his disability, a little agitated and somewhat confused. Neurologic examination a few hours later, during which time he had improved considerably, showed much difficulty in co-ordination and in use of the right arm and, to a less extent, of the right leg, without any particular weakness. The reflexes of the right arm and leg were slightly

more active. The abdominal reflexes were absent on the right. The plantar reflexes were normal. No sensory disturbances could be made out, but there was definite stereognosis, more on the right than on the left. The cardiac situation was about the same, with the rate about 100.

During the course of the next five days the neurologic symptoms improved, and in the following two days he had nausea and retching without pain or fever. Digitalis was stopped. Examination of the heart showed galloping, with a slight apical systolic murmur. The sounds were weak, and the rate was 110, with slight pulsus alternans and occasional premature beats. The blood pressure was 140 systolic, 100 diastolic. The lungs were clear. He was placed in an oxygen tent. He became restless and developed marked cyanosis, the Cheyne-Stokes breathing increased, with periods of apnea lasting forty to sixty seconds, and he died four days later.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS: So far in discussing these cases I have had a perfect score — 100 per cent wrong. I am sure that this case will be no exception.

Up to ten years before the final episode, this man had had no definite evidence of heart disease. It is true that he had had numerous episodes of palpitation and possibly even paroxysmal tachycardia of unknown kind, but as everyone knows, that is a frequent finding with a normal heart. I am sure that up to that time he had had no significant heart disease.

"The PR interval was 0.24 second." In that statement lies the answer to the gallop rhythm. Gallop rhythm may or may not have a serious prognostic significance. If the gallop is the result of a weakened myocardium, it may be extremely important. On the other hand, it is well to remember that in the presence of a long PR interval the distance between auricular and ventricular contraction is increased and therefore it is often possible to hear the auricular sound as a separate sound, in which event gallop rhythm is produced. That is undoubtedly the case here because the rhythm lasted ten years, and it is unusual to have gallop rhythm due to myocardial weakness last that long. At that time there occurred the first evidence of disease of the cardiovascular system, in that he was developing hypertension and evidence of auriculo-ventricular block.

"At another examination he had a bigeminal pulse." This finding is not necessarily significant since we know that he had been subject to ectopic beats most of his life.

The electrocardiogram taken at the age of fifty-one was abnormal in that T₁ and T₂ were low. I do

not believe that the slight shift in axis to the right was significant.

I presume that the potassium iodide was given for arteriosclerosis rather than for syphilis or goiter. Whether quinidine was given to cut down on the number of ectopic beats, or whether he actually had a paroxysmal arrhythmia, such as fibrillation, I cannot say from the evidence.

The finding of pulsus alternans at the age of fifty-five was really the first definite evidence of myocardial weakness. It is an important finding as a rule, and in this case had special significance because the gallop rhythm during the first few years of observation was not the result of a weakened myocardium.

The rising pulse and the lung findings may have represented increase in cardiac failure in spite of the fact that he was kept at bed rest and given treatment. I do not know why the giving of digitalis was delayed so long unless it was thought that the lung findings were due to something else.

The cause of the attack of pain in the right leg is not apparent. He might have had thrombophlebitis giving a transitory episode of pain or possibly a small arterial embolus from the heart that set up generalized vasospasm, a not uncommon occurrence; it is possible for such a small embolus to break up subsequently and to be distributed throughout the vascular tree, leaving no evidence of arterial occlusion on subsequent physical examination.

I presume that the pain in the anterior chest was not related to breathing. The fact that he had had similar pain on the previous night, however, is evidence in favor of the diagnosis of thrombophlebitis. This might well have represented a small pulmonary embolus first to the right lung and then to the left. He had been in bed for at least two weeks before this happened, and the pulmonary episode apparently followed the development of pain in the leg. It is also possible that the dyspnea at the time of admission and the finding of rales at both lung bases represented an earlier pulmonary embolus.

It is obvious that toward the end he had some sort of destructive lesion involving the left side of the brain. It could have been an embolus but most likely was a thrombus or hemorrhage. The sudden onset and the rather rapid clearing are in favor of a vascular episode.

A few things are fairly certain. We have a patient, fifty-nine years of age, who for the last ten years of his life had had partial auriculoventricular block, and for the last three and a half years, cardiac failure. He also had several other episodes, some of which may have been embolic. That much of the story is fairly certain, but from then on to discuss the etiology is simply conjecture.

One diagnosis that might fit most of the findings is that of hypertensive and coronary heart disease.

Involvement of the coronary arteries could well explain the long duration of auriculoventricular block, which is not exceptional. The electrocardiogram is entirely in keeping with a diagnosis of coronary heart disease. It is also possible that at some time in his career the patient had had myocardial infarction, although we have no specific evidence either clinically or by electrocardiogram to support this diagnosis. One thing that made me consider that possibility was the large size of the heart. It seemed just a little too large to be explained by hypertension of mild degree, even though it had lasted for ten years. Another point that made me consider the diagnosis of myocardial infarction was the fact that he had had several episodes, more particularly the last one, suggesting embolism. An embolus could have gone to the brain from the heart wall and produced the terminal neurologic changes. Of course the embolus, if he had one, might have come from the auricle. As in every cardiac death, the question of pulmonary embolus must be considered. I cannot rule it out, although I think it is unlikely. Whether or not he had a slight degree of chronic cor pulmonale on the basis of an old embolus also cannot be decided on the evidence presented. It is possible that he had an arterial embolus at the time of his first really severe illness, when he developed pain in the legs. Where that came from is another matter for conjecture.

What else could fit in with a picture like this? In these conferences a time always comes, after the likeliest diagnosis has been considered, when one should consider unusual diagnoses. Accordingly, in this case, I think that we should at least consider a cardiac tumor. It is well known that primary cardiac tumors may produce prolongation of the PR interval, either from interference with the arterial supply or by direct pressure over a long period of time. By direct invasion of the myocardium they may also produce cardiac enlargement and congestive failure. Cardiac tumors that grow on the endocardial surface may give rise to emboli when portions of the tumor break off. It is usually not possible to make a diagnosis of tumor, especially primary tumor, unless one has been fortunate enough to note the syndrome that is caused by the tumor's projecting into the cavity of the left auricle and causing paroxysmal obstruction of the mitral orifice. In such cases patients have a characteristic dyspnea, which is present while the patient is in the upright position and disappears when the horizontal position is assumed. I do not believe, however, that the diagnosis of tumor should be seriously considered here.

The rare forms of heart disease, such as beriberi and periarthritis nodosa, do not fit too well into this long, chronic course. So I shall stick to my first diagnosis: hypertensive and coronary heart disease.

with cardiac enlargement, congestive failure and partial auriculoventricular block and possibly thrombophlebitis and pulmonary embolism, as well as cerebral embolism.

DR. PAUL D. WHITE: I saw this man several years before he died, and although I had heard from him in the meantime, I did not see him again until a few weeks before he died. I had not the faintest idea why he had auriculoventricular block. At first, the late Dr. Breed, whose patient he was, and I thought that he probably had coronary heart disease. He also had, however, a little hypertension, and I did not know how much of a role that might have played. He continued to have a slight to moderate amount of hypertension throughout the last ten years of life, and during the latter part of his life, especially the last three weeks, he had intractable congestive failure. Undoubtedly the earlier gallop rhythm, as Dr. Williams said, was due to auriculoventricular block and that is what we ascribed it to, undoubtedly presystolic at that time. Later the patient had a clear-cut pulsus alternans and extra sounds but no murmurs; we then ascribed the fourth sound early in diastole to dilatation of the heart, which was justified because he had both types of gallop rhythm. My final diagnosis agreed with that of Dr. Breed — coronary and hypertensive heart disease, with intractable failure. I thought that the cerebral vascular accidents were embolic rather than hemorrhagic.

DR. CHESTER M. JONES: Is there anything in the x-ray films of the chest that suggests pulmonary embolism?

DR. LAURENCE L. ROBBINS: Not unless what was said to have been pneumonia could have been an infarct. The films are not particularly good, and there is no follow-up to tell how the pneumonia cleared.

CLINICAL DIAGNOSES

Coronary and hypertensive heart disease.
Congestive heart failure.
Cerebral embolism.

DR. WILLIAMS'S DIAGNOSES

Hypertensive and coronary heart disease.
Congestive heart failure.
Thrombophlebitis and pulmonary embolism?
Cerebral embolism?

ANATOMICAL DIAGNOSES

Idiopathic cardiac hypertrophy: left ventricle.
Mural thrombi: left ventricle and right auricle.
Pulmonary infarction of right upper and left lower lobes.
Chronic passive congestion of liver and spleen.
Central necrosis of liver.
Right hydrothorax, slight.
Cerebral infarction, bilateral, old and recent.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: I can tell you what we found, but I am not sure that I can name the disease this man had.

In the interstices of the trabeculae carneae of the left ventricle were thrombi that were only slightly adherent to the heart muscle itself; they could easily be picked off but had definitely occurred ante mortem (Fig. 2). The heart was enlarged, weighing 550 gm., and there was hypertrophy of the left side consistent with a moderate degree of hypertension. The coronaries, however, looked quite good. There were a few slightly atheromatous plaques but no appreciable narrowing. I am fairly certain that coronary disease itself played no part in the symptoms.

DR. WHITE: Might it be possible that the small vessels supplying the auriculoventricular junctional tissues were affected?

DR. CASTLEMAN: I doubt it because the myocardium underneath these thrombi showed no evidence of old or recent infarction. There were a few small areas of fibrosis in a few sections of the myocardium throughout the heart, but we were unable to find anything that we could call an infarct, and there was no cellular infiltration, which probably rules out Fiedler's myocarditis.¹

DR. WHITE: The fibrosis I suppose was of other origin than coronary.

DR. CASTLEMAN: Yes. There was no intimal fibrosis such as one sees with a vitamin deficiency, although in these cases one often finds mural thrombi in the left ventricle wall such as were found here.

DR. WHITE: The prolongation of the PR interval might have been rheumatic in origin. Was there any evidence of that?

DR. CASTLEMAN: No.

A PHYSICIAN: Is it not unusual to have a PR interval of 0.3 second with rheumatic fever?

DR. WHITE: It is rare, but it does occur.

DR. CASTLEMAN: In the brain there was an old linear infarct in the right temporoparietal region.

The recent episode was a hemorrhagic infarct on the left parietal region, undoubtedly due to an embolus from the left ventricle.

DR. WHITE: Every year we have at least one case of heart disease of unexplained origin. I suppose that this is the one for this year.

DR. WILLIAMS: How about the duration?

DR. CASTLEMAN: That is against it. I believe that in the longest case of Fiedler's myocarditis the patient survived only eighteen months. Also, this man was well nourished and showed no evidence of a vitamin deficiency.



FIGURE 2.

DR. CASTLEMAN: No; several months ago we had one that was similar to this — a patient with emboli to the mesenteric vessels from cardiac mural thrombi.²

DR. WHITE: It hardly seems as if hypertension alone could have explained the clinical picture.

DR. CASTLEMAN: The gross appearance of the heart fits with Fiedler's myocarditis or beriberi heart.

Mural thrombi were also present in the right auricle, and there were pulmonary infarcts in the right upper and left lower lobes.

REFERENCES

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2. Case records of the Massachusetts General Hospital (Case 30111). *New Eng. J. Med.* 230:327-331, 1944.

CASE 30392

PRESENTATION OF CASE

A nineteen-year-old farmer was admitted to the hospital for study.

The patient had had pertussis, chicken pox and scarlet fever as a child but had otherwise been in good health until five months before admission, when he developed a severe sore throat and swollen

lymph nodes in the neck. He felt quite ill and remained in bed. He was said to have been treated heavily with sulfonamides, of which he apparently received "three bottles" over a period of two or three weeks. The course of the sore throat was apparently not altered by the medication, and "the tonsils sloughed out." Either immediately after the drug was stopped or three to five days later, he suddenly developed itching all over the body, with

swelling of the neck and ankles and a blister on the wrist. No more sulfonamide was given. The swelling subsided in three days, and he slowly recovered in the following two or three months. He was able to work on the farm but he noted progressively increasing generalized fatigue. During the entire period he was under the observation of his family physician, who informed his mother that from time to time the patient had some albumin in the urine. There was no definite statement as to when albuminuria was first noted, and the amount was said to be "not alarming." He had received some liver and iron and had been told by his physician that he was improving and that his blood pressure was falling. Three weeks before admission, because of generalized aches, he went to bed, where he remained. One week later he developed bleeding and soreness about the base of the glans penis, and four days before entry he began to have tenesmus and bloody oozing from the rectum. There was one episode of vomiting the day before admission. He had lost a total of 20 pounds. There was no gross hematuria, increased frequency, nocturia or dysuria.

Physical examination showed a well-developed, slightly pale, chronically ill young man who was too weak to sit up. There were occasional questionable petechial lesions on the outer aspect of the left thigh. A large exudate was seen in the left fundus; the vessels were thin and there were no hemorrhages. The tongue was dry and coated. The breath was slightly uriferous. The pharynx was moderately injected. The tonsils were small. The left border of cardiac dullness was felt 8.5 cm. from the midline. The sounds were of good quality and regular. Grade 1 apical and pulmonic systolic murmurs were heard. The lungs were clear. The abdomen was normal. There was partial hypospadias involving the glans; and a bleeding ulcer under the foreskin behind the glans. There were a few small hemorrhoids. A coarse tremor was brought out by exercise, and there was a rare spontaneous muscle twitch. The Chvostek and perineal reflexes were negative. The tendon reflexes were feeble, with a tendency to reduplication. The plantar reflexes were diminished. The sensorium was intact.

The blood pressure was 120 systolic, 75 diastolic. The temperature was 99.2°F., the pulse 86, and the respirations 20.

Examination of the blood showed a red-cell count of 2,530,000, with 8 gm. of hemoglobin. The white-cell count was 7400, with 87 per cent neutrophils. A blood Hinton test was negative. The urine was cloudy, with a pH of 5.5, a specific gravity of 1.010 and a +++ test for albumin; the sediment contained 4 to 5 white cells, 15 to 20 red cells and rare granular and red-cell casts per high-power field and many triple phosphate crystals. The stools were guaiac positive.

A roentgenogram of the chest was negative.

The blood nonprotein nitrogen was 100 mg. per 100 cc. The carbon dioxide combining power was 19.5 millimols per liter, and the chloride 90.9 milliequiv. The uric acid was 14 mg. per 100 cc., and the blood protein 8.4 gm., with an albumin of 4.0 gm. and a globulin of 4.4 gm., an albumin-globulin ratio of 0.9. The calcium was 11.4 mg. per 100 cc., the phosphorus 22.2 mg., and the phosphatase 4 Bodansky units. The last three determinations were done on hemolyzed blood, and a repeat test for phosphorus gave a level of 16.0 mg. per 100 cc. The phenolsulfonephthalein excretion was less than 5 per cent at the end of two hours.

The patient received daily intravenous fluids, including sodium lactate. His condition steadily became worse. On the third day the nonprotein nitrogen was 128 mg. per 100 cc. For the first three days the urinary outputs were 1000, 1500 and 2000 on an intake of 1250, 2000 and 3700 cc., respectively. The character of the urine remained the same except that the pH rose to 7.5. The blood pressure was 140 systolic, 80 diastolic. On the sixth day he became semicomatose and had frequent muscle twitches. Ulcers developed in his mouth and extended into the pharynx. There were edema and swelling of the perioral tissue. The stools gave a +++ test for guaiac, and there was a discharge of serosanguineous fluid from the oral cavity. His pulse rose to 120. The lungs, however, remained clear and the heart sounds were of good quality. The following day the urinary output fell to 500 cc. on an intake of 4500 cc. On the afternoon of that day the blood pressure fell to 110 systolic, 30 diastolic, and the pulse was 100; the patient died shortly thereafter.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM BECKMAN: All the information in the record adds up to the fact that this man died of renal failure. From the history we learn that he had had albumin in his urine and that his blood pressure must have been elevated since his physician said it was falling. The bleeding tendency, the weight loss and the aching are also consistent with uremia.

The physical examination also provides evidence for the diagnosis of renal failure. The retinal exudate and the tremor are frequent findings, and petechial lesions are occasionally seen in uremia. Of course in the terminal stage of the disease one would have liked to note a higher blood pressure, but the normal values discovered in the hospital are certainly not incompatible with the condition.

The laboratory data confirm the impression of renal failure. Anemia is an almost constant feature, as are albuminuria and the finding of red cells and casts in the sediment. The elevated nonprotein nitrogen, the acidosis, — as evidenced by the diminished carbon dioxide combining power, — the

elevated uric acid and the marked increase in phosphorus concentration, all point toward markedly diminished renal function. I believe that with this array of evidence no other diagnosis can be supported.

Other causes of an elevated nonprotein nitrogen, such as dehydration and severe diarrhea, would not exhibit all the findings in the history and physical examination, and of course he did not have diarrhea.

Having now made out a case for renal failure, the important part of this exercise is to try to decide on the etiology of the kidney disease that was present. Of course any form of renal disease, from glomerulonephritis to amyloidosis, can lead to uremia, and it is usually difficult to tell precisely which one is present in any given case. It seems possible to rule out amyloidosis because there was no evidence of any condition, such as chronic suppuration, rheumatoid arthritis or tuberculosis, that is commonly associated with amyloidosis. Likewise one can rule out chronic pyelonephritis, since there was no evidence of an infection of the urinary tract; at least there is no report of a positive urine culture.

My first suggestion is that the streptococcal infection that he suffered five months prior to admission gave rise to an acute glomerulonephritis that remained active until death. I have no way of ruling out this possibility, but I should not expect acute nephritis to subside for a brief period and then flare up again. From the record one cannot be absolutely certain that there was a remission with a relapse, since his physician apparently found an elevated blood pressure during the period when he was well and able to work.

A second possibility is that following the scarlet fever that he had as a child he developed an acute glomerulonephritis, which had been smoldering in a latent state up to the time of the infection that precipitated the present illness. The latter infection may have exacerbated the already present nephritis and produced this picture of chronic renal failure.

A third possibility is that this patient's renal disease was the result of a reaction to the sulfonamides that he was given in fairly large quantities. A sulfonamide reaction is the only interpretation that I can think of for the attack of itching of the skin and swelling of the ankles. It has been amply demonstrated in the past few years that the sulfonamides are capable of producing renal disease, which is, I believe, of a somewhat variable nature. Rich* has reported some cases in which the patients developed periarteritis nodosa, presumably as a result of the hypersensitivity to the sulfonamide. The fact that this man had such marked muscular aching might be explained on the basis of periarteritis nodosa. Also, the petechial rash is more consistent with this diagnosis than it is with plain uremia.

Finally, it is possible that a latent nephritis, which occurred at the time of the scarlet fever, could be exacerbated not only by the streptococcal infection but also by the sulfonamide reaction.

I have no way of differentiating the last four possibilities that I have mentioned. However, making use of the meager clinical data that I have, I shall commit myself to a diagnosis of sulfonamide reaction with resultant periarteritis nodosa.

CLINICAL DIAGNOSIS

Chronic glomerulonephritis.

DR. BECKMAN'S DIAGNOSIS

Sulfonamide nephropathy, with resultant periarteritis nodosa and renal failure.

ANATOMICAL DIAGNOSES

Chronic glomerulonephritis, with superimposed acute pyelonephritis.

Sulfonamide nephropathy?

Balanoposthitis, acute and chronic.

Cystitis.

Parathyroid hyperplasia, secondary.

Bronchopneumonia.

Petechial hemorrhages of lungs, stomach and esophagus.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this boy showed a small pair of kidneys, weighing 100 gm., thus indicating that the renal disease dated back for a long period of time — certainly longer than five months. Microscopic examination showed marked dilatation of the tubules, which is the best anatomic evidence that we have of renal impairment of any type. The changes in the glomerular tufts were characteristic of chronic glomerulonephritis, with numerous capsular adhesions. In addition there was a fair amount of lymphocytic and polymorphonuclear infiltration and fibrosis of the stroma.

How much the sulfonamides had to do with this uremic death is difficult to answer. There is no doubt that he received sulfonamides after his kidneys had contracted, and the drug must have been an added burden to the kidneys, which might have precipitated the acute renal failure. We have no definite evidence in the kidneys, however, that this was the case, and the findings are consistent with a chronic glomerulonephritis and a superimposed acute infection. The patient did have a mild cystitis, and further evidence that he had had renal disease for a long time was a moderate degree of secondary hyperplasia of all four parathyroid glands.

The heart was slightly enlarged and weighed 330 gm.

*Rich, A. R., and Gregory, J. E. Experimental demonstration that periarteritis nodosa is manifestation of hypersensitivity. *Bull. Johns Hopkins Hosp.* 72:65-88, 1943.

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COMPENSATION FOR EMERGENCY CARE IN CASES OF INDUSTRIAL INJURY

THIS issue of the *Journal* carries a communication from the Secretary that deserves the notice of all the members of the Massachusetts Medical Society, particularly those who occupy regular positions on a hospital staff. Heretofore the right of staff physicians to compensation for services rendered those injured in industry has been challenged by many insurance companies. Their refusal to pay for such services was based on certain decisions of the Massachusetts Supreme Court. These decisions seem to have arisen out of the Court's interpretation of the law as it relates to hospitals and to the principle of free choice of physician as provided for in the Massachusetts Workmen's Compensation Act.

The layman reading these decisions is led to believe that the Court regards hospitals as merely asylums for the poor. Although it is true that the law frequently lags a bit behind what has come to be regarded by the people as established social practice, it seems incredible that it should lag so far behind as not to recognize what everybody, for a long time, has come to accept as the hospital's function in the scheme of American life. The present-day hospital serves the whole community without any loss of emphasis on its original purpose. It has done this as the result of public demand, in keeping with scientific progress and a changing way of life.

The Workmen's Compensation Act was established for the purpose of protecting the workman and his family from the hazards of industry. When the workman ran afoul of these hazards, the responsibility for his care was placed by law on industry itself, as a legitimate addition to the costs of production. It is little wonder, then, that many physicians are bewildered by these decisions of the Court, which put doctors in the position of sharing costs that are imposed elsewhere by the law. Mrs. Tousant, the able chairman of the Massachusetts Industrial Accident Board, has expressed, in conference with the Committee on Public Relations of the Society, the Board's dissatisfaction with the way in which many industrial injuries have been handled. She is agreed that the confusion caused by the issues discussed here may be partly responsible.

The agreement reported elsewhere in this issue is the result of many conferences held by the Massachusetts Industrial Accident Board with the Medical Advisory Committee of the Board, a subcommittee of the National Council of Claims Executives on Compensation Insurance and a subcommittee of the Committee on Public Relations of the Massachusetts Medical Society. Drs. Daniel J. Ellison, David D. Scannell and Gordon M. Morrison, who comprise the latter subcommittee, deserve the sincere thanks of the Society.

This agreement has done much to clear the air, and it is the obligation of every hospital-staff physician to see to it that the confidence of the Industrial Accident Board has not been misplaced.

SHORTAGE OF NURSES STILL ACUTE

FOLLOWING a summer in which the war news became increasingly good, the needs of the military services for nurses have grown steadily more acute. The victories that are winning the war are taking their toll, on every front, in casualties. All the nurses actively taking part in the combat areas abroad and in the military hospitals at home and many of those in other types of foreign service are reaching the point where they themselves need relief. With the present plan for releasing those who cannot continue under the strain and for giving leave to those who have had long stretches of service, the need for additional enlistments continues.

According to official reports, the New England states were 120 short of meeting their quota of 1023 for the first half of the year, although both Massachusetts and Rhode Island went well over their state quotas. They are now asked to provide 1000 more nurses during the last part of 1944, at least half of them by November 1. The Massachusetts quota — 526 — is naturally the largest.

Most of these enlistments must come from new and recent graduates. It is expected that at least 30 per cent of the new graduates from the schools of nursing will be available for military service, 50 per cent for essential civilian service, and perhaps 15 per cent — those specially qualified — for post-graduate study. No recent graduate will be fulfilling her professional obligation at this critical time if she enters private-duty nursing or office nursing, both of which must be cut to the minimum until the acute shortage is relieved.

Although some institutions and agencies seem to have weathered their worst periods of shortage, others find things more and more difficult with each passing month. This is particularly true of some of the hospitals without schools of nursing, which are in extreme need of head nurses, supervisors and nurses for the general staff. If, as now seems apparent, the general military hospitals, such as the Cushing, the Lovell and the Edwards, here in Massachusetts are also going to need civilian nurses for the next few months to supplement the staff of Army nurses, then there is no likelihood

that the efforts to see that nursing service is equitably distributed to meet the most essential need can be relaxed.

It is important for every physician to know the situation and to use his influence to restrict the use of nurses in private cases or noncritical office work until the needs of the armed forces and civilian hospitals are adequately met.

MASSACHUSETTS MEDICAL SOCIETY SECRETARY'S OFFICE

It seems important that those of our members who occupy staff positions in Massachusetts hospitals should have called to their attention in this special manner an agreement that has just been concluded through the aegis of a subcommittee of the Massachusetts Medical Society appointed to confer with the Medical Advisory Committee of the Industrial Accident Board. The subject on which this agreement has been reached has been a source of contention over the years. The elimination of this contention should pave the way for better care of those injured in industry and for a better understanding between all concerned.

The report of Drs. Daniel J. Ellison, David D. Scannell and Gordon M. Morrison, which ably and clearly set forth this agreement and the manner in which it may be maintained, is as follows:

This report is a follow-up in a matter on which a preliminary report was made one year ago.

This committee was appointed at the request of the Industrial Accident Board to recommend procedures whereby the medical care and surgical care of the injured workman might be improved. It was and still is the opinion of this committee that the surgical staffs of recognized hospitals, by and large, represent the men in any given community most able to cope with surgical conditions.

Our first procedure was to attempt to make these men more willing to care for or handle industrial accident cases while they were on duty on ward service. To this end, through the co-operation of the chairman of the Industrial Accident Board, it has now been agreed by all the insurance companies handling this type of business that the man rendering emergency treatment to an injured workman shall be paid for such treatment. In defining first-aid treatment it may be said that emergency treatment ranges from simple first-aid to an extensive operation for the relief of a compound fracture. Reasonable charges submitted by any registered physician in this state will be honored. There shall be no change in the relation between the patient and the hospital-staff physician as it now exists in the various hospitals of the Commonwealth. The problem of the surgeon on duty caring for an injured employee in the ward without being paid except for the emergency treatment cannot be solved by any method except the passage of an amendment to the law by the General Court providing for the payment for such services or a reversal of the ruling previously made by the Supreme Court. It is the opinion of the committee that, whereas surgeons on ward service render equally as able care to both ward and private patients, it might be well to institute proceedings that would change this rather unfortunate state of affairs.

Payment will not be made for services rendered by interns or residents but for work actually done by surgeons

recognized by a hospital, whether or not on duty. This we believe to be a step forward in the better care of the injured workman.

It is also agreed that the injured employee, if conscious, shall be offered two lists of physicians, — one a list of staff doctors selected by the insurer and the other a complete list of the members of the hospital staff, including the courtesy staff, — with the understanding that the employee has a free choice of any doctor on either of these lists. On the other hand, should the injured employee choose as his physician a doctor connected with some hospital other than the one to which he has been taken he may be removed without prejudice to that hospital, where the physician of his choice may care for him.

Your committee believes that it is impossible to prevent a certain number of these patients being taken to unaccepted hospitals and being cared for by men of limited ability, but that the solution of this part of the problem lies in an educational program designed to teach people the difference between recognized and unrecognized hospitals. The problem is not so simple as it seems at this time owing to the absence of many of the best men in the service and to the fact that their places have been taken by men of considerably less maturity in judgment.

There is one other arrangement that has recently been concluded that in some cases may obviate this difficulty. Through an agreement with the Blue Cross, an injured employee insured under the Blue Cross may be transferred from a ward to a semiprivate or private room and the difference in expense will be paid by the Blue Cross, making such an employee the private patient of the surgeon on duty or of the surgeon chosen by the employee.

It is further thought that freedom of choice of physician by the injured employee should at no time be interfered with.

It is the desire of the chairman of the State Industrial Accident Board that a committee of this type be continued.

This agreement should be studied carefully, and every assistance should be given to Massachusetts hospitals by their respective staff members in putting its provisions into practice.

The Industrial Accident Board has already addressed the hospitals in this same vein.

MICHAEL A. TIGHE, *Secretary*

DEATHS

FAULKNER — Herbert K. Faulkner, M.D., of Keene, New Hampshire, died September 15. He was in his eighty-sixth year.

Dr. Faulkner received his degree from Harvard Medical School in 1885 and practiced in Keene for forty years before retiring in 1920.

Five daughters and two sons, one of whom is Captain James M. Faulkner (MC), U.S.N.R., survive.

OUTHOUSE — John S. Outhouse, M.D., of Shelburne Falls, died June 20. He was in his seventieth year.

Dr. Outhouse received his medical degree from McGill University, Montreal, in 1898.

His widow, one daughter and two grandchildren survive.

SHERMAN — Frank M. Sherman, M.D., of West Newton, died September 14. He was in his eighty-eighth year.

Dr. Sherman received his degree from Harvard Medical School in 1881. He had retired several years ago.

His widow, two sons and a daughter survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINIC FOR CRIPPLED CHILDREN

CLINIC	DATE	CLINIC CONSULTANT
Salem	October 2	Paul W. Hugenberger
Haverhill	October 4	William T. Green
Lowell	October 6	Albert H. Brewster
Pittsfield	October 16	Frank A. Slowick
Springfield	October 18	Garry deN. Hough, Jr.
Brockton	October 19*	George W. Van Gorder
Worcester	October 20	John W. O'Meara
Fall River	October 23	Eugene A. McCarthy
Hyannis	October 24	Paul L. Norton

*Date changed.

WAR ACTIVITIES

INDUSTRIAL HYGIENE

A HEALTH PROGRAM FOR SMALL INDUSTRIES

A campaign for the advancement of industrial health in the small industries of the Detroit area is being sponsored by the Wayne County Medical Society. The main objective is to provide emergency care in these plants and eventually to convince the management that a health program is not costly but economically profitable, even though it necessitates an initial expenditure for first-aid stations and certain equipment.

When a sufficient number of doctors have notified the society of their availability to assist in the program, letters will be sent by the medical society to industries in the area employing 25 to 1000 workers that do not employ a full-time plant physician. The City of Detroit Department of Health has offered to render service or advice regarding occupational diseases found in these plants.

The plan proposes meetings at regular intervals, in each plant, of the president or plant manager, the plant doctor or his appointed representative, the plant or visiting nurse, the first-aid man, the director of the safety committee, a representative of the employees and the personnel or employment manager. Suggested topics for these meetings include: disabilities from accidents; first-aid at the plant; physical examination and health of the worker; noncompensable illnesses such as colds, other infections and surgical disabilities; co-operation of the family physician in cutting down loss of workdays; ventilation and sanitary conditions in the plant; nutrition of the workers and food conditions; and contagious diseases and co-operation with the public-health department. — Reprinted from *Industrial Hygiene News Letter* (August, 1944).

CORRESPONDENCE

CASH BENEFITS

To the Editor: The editorial "Massachusetts EMIC Program" in the September 7 issue of the *Journal* was interesting and timely. It called to mind an editorial appearing in the January 20, 1938, issue of the *Journal*, entitled "Group Health Association, Incorporated." That editorial questioned the wisdom of the American Medical Association's opposition to Group Health Association, Washington, D. C., and suggested that the manner in which the medical profession reacted to medical-service plans was of vital importance to physicians. The subsequent decision of the Supreme Court of the United States concerning the opposition of the American Medical Association and the unfortunate publicity that accrued to the medical profession seem to have amply supported the former editorial comment.

In the present instance the American Medical Association has again taken action that may be detrimental to physicians. It has recommended that the cash allotment method of dis-

bursing funds under the EMIC program be substituted for the present method of directly paying physicians for the services they render. The advocacy of such cash benefits by the profession may lead the public to believe that physicians approve the expenditure of the public's money under the pretext of medical care without concern whether or not that money is actually spent on medical care. The public may also infer that the profession is not concerned about the quality of medical care purchased with government funds. Finally, the public may conclude that doctors wish to be in a position to negotiate with each of these mothers the fees that they should pay and thus disregard the decision of Congress to free such mothers from the worries of medical expense.

If the public should feel that doctors are more concerned with protecting the present system of medical practice than in economically distributing the cost of medical care and improving its quality, then the public is likely to pay little attention to the advice of the profession in the consideration of programs for the improvement of medical care. Thus it would seem that the advocacy of cash benefits by the official bodies of the medical profession is a matter of importance to physicians, for they suddenly may find that their official representatives have once again subjected the medical profession to public criticism.

ALLAN M. BUTLER, M.D.

Massachusetts General Hospital
Fruit Street
Boston 14

BOOK REVIEWS

Psychiatry in War. By Emilio Mira, M.D. 8°, cloth, 206 pp., with 6 figures. New York: W. W. Norton & Company, Inc., 1943. \$2.75.

Mira, a former professor of psychiatry in Barcelona, served during the Spanish Civil War as an active physician in the treatment of mental diseases in the Republican Army. His account is by far the best that has been written on psychiatry during this war and is of outstanding value because of its clear picture of the effects of war on the mind of man. The book forms a fitting introduction to the treatment of the many neuropsychiatric problems that are appearing in World War II, and this timely contribution will be welcomed by all physicians who have to do with the care of the American soldier mentally disturbed by war conditions. There are excellent chapters on the effect of bombing on the civilian population, in addition to the case histories and personal experience of the author at the front. The morale of an army under stress is given particular consideration.

The author is well known in this country, having delivered addresses here in 1933 and more recently being the Salmon Lecturer at the Academy of Medicine, New York City. The book comprises the latter lectures, plus additional material, particularly on the diagnostic apparatus devised by the author for estimating the fitness of a person to serve in the Army. This apparatus, which Mira believes is an efficient means of military selection, is now being used for investigation in this country.

The book is an important landmark in military psychiatry for it contains material not found elsewhere. It is well written and factual, and the conclusions should have a wide field of application both in military and in civilian life.

The Conquest of Epidemic Disease: A chapter in the history of ideas. By Charles-Edward A. Winslow, Dr.P.H. 8°, cloth, 411 pp. Princeton, New Jersey: Princeton University Press, 1943. \$4.50.

This volume may well be considered a classic. It approaches the problem of the history of the attack on epidemic diseases with a point of view that differs from other writings. In part it is medical history; in part an anthology of the writings of the makers of that history; and in part the clear thinking of C.-E. A. Winslow. The author has attempted to depict how the leaders of medical science visualized their problems. So far as possible he has told their story in their own words, and has so woven them into the text that at times, without quotation marks, it is difficult to separate the original writer from his historian. The field of epidemic disease is unfolded from the days of the Old Testament

down through the ages to Charles Value Chapin, Francis Torius, Rush, Panum, Budd, Snow, Pasteur, Koch and many others are reviewed by their thoughts rather than by their acts.

Winslow calls his work "a chapter in the history of ideas." It seems more than that. The ideas of the masters are integrated and interpreted by a master. This volume is not a textbook and may not be suited to the library of the entire medical profession but it will be a delight to those interested in medical history, to those trying to learn more regarding human understanding, to the busy doctor desirous of spending a quiet evening before the fireside and to a limited number of public-health workers, both medical and nonmedical.

The Genealogy of Gynaecology. By James V. Ricci, MD 4°, cloth, 578 pp., with 53 illustrations. Philadelphia: The Blakiston Company, 1943. \$8.50.

This is an authoritative, scholarly and well-documented history of gynecology from its remotest archaic beginnings through the Assyrian, Babylonian, Egyptian and Hindu epochs, the classic Graeco-Roman age, the Talmudic, Byzantine and Arabic eras and the Middle Ages and Renaissance to the end of the eighteenth century. From all these epochs there is an abundant bibliography and the reproduction of fifty-three well-selected illustrations, chiefly of gynecologic instruments and of developing anatomical concepts. In his preface, as in his gracious dedication to the Harvard Medical School, the author freely acknowledges his indebtedness to previous writers but modestly underestimates the wide ranging and painstaking research that the accumulation of his material must have required. His work is a priceless gift to the profession, and one waits with eager anticipation for the subsequent volume, promised in the introduction by Dr. Schumann, of Philadelphia, covering the period of the nineteenth century.

Reaction to Injury: Pathology for students of disease based on the functional and morphological responses of tissues to injurious agents. By Wiley D. Forbus, M.D. 4°, cloth, 791 pp., with 532 illustrations, 20 of which are in color. Baltimore: Williams & Wilkins Company, 1943. \$9.00.

Forbus's new textbook of pathology follows the arrangement that has been made familiar by MacCallum's book—an etiologic compilation based on the type of injury causing disease. The present volume contains introductory material, a brief chapter on the history of pathology, a classification of the causes of disease and a full discussion of infectious diseases. The author states that a second volume covering the other fields of pathology is in preparation but that the importance of infectious diseases in wartime makes the publication of the first volume worth while at the present moment.

The discussion of the topics within the scope set for the work as it now stands is more complete than in most pathology texts, such as those of Boyd and Karsner. The presentation of material is clear and critical; both sides of controversial questions are given, and dogmatic statements are meticulously avoided. The pathology of the various infectious diseases is set in relation to the picture of the diseases as wholes, and an adequate basis for the difficult transition from preclinical to clinical studies is provided. This has been accomplished to a certain extent at the sacrifice of considerations of disease as a biologic phenomenon, particularly in its relation to biochemistry.

There are many advantages in the arrangement of a text according to the type of injury causing disease. These accrue chiefly from the fact that etiology receives the emphasis that it deserves, yet it often separates by hundreds of pages subjects that should be considered together. For instance, Forbus discusses glomerulonephritis among the acute and chronic, nonsuppurative inflammatory processes, whereas vascular diseases of the kidneys will be considered in the volume that has not yet appeared. "You pay your money and take your choice."

The illustrations are definitely superior to those of most texts of pathology now in general use. The photographs of gross specimens are excellent, as are most of the photomicrographs. Some of the latter could be improved by procuring better fixed and stained preparations (for example, Figs. 309,

345 and 508). The colored plates are made from Kodachromes of varying merit.

References follow each chapter. These are well chosen from the student's viewpoint but are considerably out of date, few of them being more recent than four years before publication of the volume. In some instances, later material is included in the text than in the bibliography.

Within the fields covered by this volume, the text is one of the best now available. It will appeal to the better students, which is as it should be, and to those clinicians and pathologists who wish a reference work on the pathology of infectious diseases. Forbus's book is a welcome change from the numerous textbooks of pathology that are little more than catalogues of disease. Without supplementation by another text, it lacks too many important topics (for example, arteriosclerosis and tumors) to make it suitable for a second-year course in pathology as it stands.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return or the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Office Treatment of the Nose, Throat and Ear. By Abraham R. Hollender, M.D., associate professor of laryngology, rhinology and otology, University of Illinois College of Medicine, and otolaryngologist, Research and Educational Hospitals, Chicago. 8° cloth, 480 pp., with 33 illustrations. Chicago: The Year Book Publishers, Incorporated, 1943. \$5.00.

This manual is written for the purpose of furnishing details of office treatment not usually found in prescribed college curriculums or in the training provided for residents in hospitals. The work is divided into two sections: the first discusses the general therapeutic methods used in all diseases of the upper respiratory tract, and the second considers the various diseases of the nose, sinuses, mouth, larynx and ear.

The Religious and Philosophical Aspects of van Helmont's Science and Medicine. By Walter Pagel. 4°, paper, 44 pp. Baltimore: The Johns Hopkins Press, 1944. \$1.00.

In this monograph an attempt is made to define the position of van Helmont in the history of philosophy.

Safe Convey: The expectant mother's handbook. By William J. Carrington, M.D., attending gynecologist, Atlantic City Hospital, Atlantic County Hospital for Nervous and Mental Diseases, Pine Rest Hospital, Atlantic City Municipal Hospital and Atlantic Shores Hospital. 8°, cloth, 256 pp. Philadelphia: J. B. Lippincott Company, 1944. \$2.50.

This manual of personal hygiene for the expectant mother has been written by an obstetrician of large experience. One third of the volume is devoted to the care of the newborn infant. The foreword comprises a short history of obstetric books for the laity.

Minor Surgery. By Frederick Christopher, M.D., associate professor of surgery, Northwestern University Medical School, Chicago, and chief surgeon, Evanston (Illinois) Hospital. Fifth edition. 8°, cloth, 1006 pp., with 575 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. \$10.00.

The text of this edition has been thoroughly revised; many sections have been entirely rewritten, and many new sections have been added. The subjects of wound healing and treatment have been rewritten with particular attention to the local use of sulfonamides, and the administration of penicillin is discussed. The employment of plastic casts in wound treatment is considered. The section on burns has been extensively revised and includes consideration of the use of nonadherent pressure dressings and of plasma administration. A new chapter on preoperative and postoperative care has been added. This includes the following topics: shock and its treatment with blood plasma and other agents; dehydration; hypoprothrombinemia; vitamin deficiency (including vitamin K); preoperative preparation in special

cases; water balance; electrolyte requirements; protein requirements and treatment of hypoproteinemia with amino acids; the use of the Miller-Abbott tube; postoperative pulmonary complications; prophylaxis and treatment of postoperative thrombosis and embolism (including the use of heparin and dicumarol); and postoperative urinary complications (including the use of sodium lactate to increase the pH of the urine during administration).

New subjects considered or emphasized for the first time are tetanus toxoid, new developments in the treatment of varicose veins, ligation of the femoral vein in thrombophlebitis, treatment of pilonidal sinuses, wire sutures in tenorrhaphy, the hanging cast in fractures of the humerus, x-ray treatment for sprained ankles, "paratrooper fracture," walking casts, sternal infusions, treatment of cardiac arrest and employment of intravenous anesthesia.

This authoritative treatise, first published in 1929, should prove of great value at the present time to physicians who are called on to treat minor surgical conditions.

The Hippocratic Oath: Text, translation and interpretation. By Ludwig Edelstein. A supplement to the *Bulletin of the History of Medicine*. 4°, paper, 64 pp. Baltimore: The Johns Hopkins Press, 1943. \$1.25.

The text of the oath is given in both Greek and English. In his interpretation Dr. Edelstein has scrutinized the text, sentence by sentence, and has made extensive use of the writings of ancient authors in his inquiries. The covenant, which precedes the code, and the ethical code are considered separately. The two final chapters discuss the unity of the document and the date and purpose of the oath. This scholarly presentation should be on the shelves of every library.

Health for the Having: A handbook for physical fitness. By William R. P. Emerson, M.D., medical consultant in physical fitness, Aetna Life Insurance Company. 12°, cloth, 146 pp., with 6 illustrations. New York: The Macmillan Company, 1944. \$1.75.

This small manual has been written for the layman, and much emphasis is placed on body weight and personal hygiene. Correct diet is stressed and valuable tables of calories and weight and height are appended to the text.

Physical Foundation of Radiology. By Otto Glasser, Ph.D., professor of biophysics and head of Department of Biophysics, Cleveland Clinic Foundation, Cleveland; Edith H. Quimby, Sc.D., associate professor of radiology (physics), College of Physicians and Surgeons, Columbia University, New York; Lauriston S. Taylor, Ph.D., chief of X-ray Section, National Bureau of Standards, Washington, D.C.; and J. L. Weatherwax, M.A., Philadelphia General Hospital and Graduate School of Medicine, University of Pennsylvania, Philadelphia. 12°, cloth, 426 pp., with 95 illustrations and 53 tables. New York: Paul B. Hoeber, Incorporated, 1944. \$5.00.

This combined work of four authors is an attempt to provide a teaching text in the field of radiologic physics. The manual has been designedly written in an elementary and nonmathematical character. General bibliographies and special references are appended to each chapter for the purpose of furnishing material to teachers who may desire to supplement the text with other material. Throughout the book the place of radiologic physics as a part of modern physics has been kept in mind. There is a special chapter on therapy records, which is amplified by extensive tables of dosage data for both x-rays and radium. The first chapter, which is historical, contains valuable chronologies from the time of Gilbert in 1600 to Kerst in 1940. These tables make the manual invaluable to all those interested in the history of medicine and physics. The book is well printed with a good type and is of a convenient size to handle.

NOTICES

TUFTS POSTGRADUATE COURSES FOR THE GENERAL PRACTITIONER

The Postgraduate Division of Tufts College Medical School has recently announced a series of courses designed for the busy general practitioner who wishes to bring his knowledge up to date. The work is largely given in the New England

Medical Center (Boston Dispensary, Joseph H. Pratt Diagnostic Hospital, Boston Floating Hospital and Tufts College Medical School). Facilities of other hospitals in and around Boston are also available in several of the courses.

Graduates of approved medical schools are eligible for admission to any of the courses. Graduates of other medical schools may be admitted if considered acceptable. Such applicants should submit evidence that they are members of their state medical societies. Applications for admission and requests for further information should be made to the Chairman, Postgraduate Division, Tufts Medical School, 30 Bennet Street, Boston.

Tuition fees are payable on the opening day of each course. In addition, a \$5.00 registration fee covers all courses taken within a twelve-month period and is due on acceptance for study. The registration fee will be forfeited in cases of withdrawal without notification.

Through the Bingham Associates Fund, fellowships for postgraduate study are available for physicians practicing in Maine who are members of the Maine Medical Association. Application should be made to the Chairman. These fellowships are not available to physicians from other parts of New England; the tuition fees, however, are placed at a level calculated to make the courses available to the great body of physicians in New England.

For a limited number of physicians, room and board are available at the New England Medical Center. Rates for room are \$10.00 double and \$12.00 single per week. Meals are available through the purchase of meal tickets. Reservations for room accommodations *must be made* in advance and should be addressed to Mr. Frank E. Wing, Director, Boston Dispensary, 25 Bennet Street, Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

A number of changes in regulations and requirements were put into effect at the last annual meeting of the American Board of Obstetrics and Gynecology. These were designed to aid civilians as well as candidates in the service. Among these is the waiver, temporarily, of the requirement of the American Medical Association for men in the Army or Navy, especially for those who proceeded directly or almost so from hospital into military service, on a statement of intention to join promptly on return to civilian practice. At this meeting the Board also decided to accept a period of nine months as an academic year in satisfying the requirement for certain years of training. This is only for the duration and even men who are not eligible for military service but who are nevertheless in hospitals where the accelerated program is in effect have been allowed to submit this short-time period of training in lieu of the previous requirements.

Beginning with the next written examination, which is scheduled to be held on the afternoon of February 3, 1945, the Board will limit the written examination to a maximum period of three hours, and in submitting case records, all obstetric reports that do not include measurements, either by calipers and, as indicated, by acceptable x-ray pelvimetry, will be considered incomplete.

Prospective applicants or candidates in military service are urged to obtain from the office of the Secretary a copy of "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards," which will be supplied on request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the offices of the Surgeons-General, having been recommended to the services in a Circular Letter No. 76 from the War Department Army Service Forces, and referred to as the "Medical Officer's Service Record." These will enable prospective applicants and candidates to keep an accurate record of work done while in military service and should be submitted with the candidate's application, so that the Credentials Committee may have this information available in reviewing the application.

Applications and a bulletin of detailed information regarding the Board requirements will be sent on request to the Secretary's Office, 1015 Highland Building, Pittsburgh 6.

Applications must be in the office of the Secretary by November 15, 1944, ninety days in advance of the examination. The time and place of the Spring 1945 (Part II) examination will be announced later.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, October 5, in the classroom of Nurses' Residence at 7:15 p.m. A motion picture on cat anesthesia will be shown. Dr. Mabelle C. Hiscock will be chairman.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 5

- THURSDAY, OCTOBER 5
7 15 p.m. New England Hospital for Women and Children
- SATURDAY, OCTOBER 7
*10 00-11 30 a.m. Medical staff rounds Peter Bent Brigham Hospital
- MONDAY, OCTOBER 9
*12 15-1 15 p.m. Clinicopathological conference Peter Bent Brigham Hospital
- TUESDAY, OCTOBER 10
*12 15-1 15 p.m. Clinicoröntgenological conference Peter Bent Brigham Hospital
- WEDNESDAY, OCTOBER 11
*12 00 m. Clinicopathological conference Children's Hospital
- *Open to the medical profession

OCTOBER 2-5 Second Wartime Public Health Conference Page 4, issue of September 21

OCTOBER 2-7 Seminar in Legal Medicine, Harvard Medical School Page 110, issue of July 20

OCTOBER 3-5 American Public Health Association. Page ix, issue March 30

OCTOBER 9-20 1944 Graduate Fortnight of the New York Academy of Medicine. Page xvii, issue of July 27

OCTOBER 10 New England Society of Anesthesiology. Page xvii, issue of September 7

OCTOBER 13 Mental Conditions Resulting from the War. Dr. C. Bonner Pentucket Association of Physicians 8-30 p.m., Haverhill

OCTOBER 16-November 3 Third Postgraduate Course in Industrial Medicine Page xix, issue of September 14

OCTOBER 30 New York Institute of Clinical Oral Pathology, New York Academy of Medicine Page 110, issue of July 20.

NOVEMBER 2-4 Association of Military Surgeons Page xvi, issue of August 17.

FEBRUARY 19 American Board of Internal Medicine Page 436, issue of September 21

DISTRICT MEDICAL SOCIETIES

SUFFOLK

DECEMBER 7 Censors' meeting

WORCESTER

- OCTOBER 11 Rutland State Hospital
NOVEMBER 8 Grafton State Hospital.
DECEMBER 13. Worcester City Hospital.
JANUARY 10. St Vincent Hospital, Worcester.
FEBRUARY 14 Worcester State Hospital.
MARCH 14 Worcester Memorial Hospital.
APRIL 11 Hahnemann Hospital, Worcester.
MAY 9 Annual meeting.

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Number 14

THE APPLICATION OF PULMONARY PHYSIOLOGY TO THERAPEUTIC PROCEDURES*

With Special Reference to the Use of Oxygen

CECIL K. DRINKER, M.D.†

BOSTON

DURING many years of experimental work in what I call mammalian or medical physiology, I have been drawn again and again to observations on the lungs and, on looking back, am struck by the diverse lines of inquiry that have been necessary. Physiology, anatomy, pathology, surgery, all have had their place, with emphasis on the fact that neither the experimenter in the laboratory nor the agent of disease can succeed in doing just one thing to the lungs. The functions, structure and functional relations of lung tissue are so vital, so delicately ordered and so immediately of consequence to other parts of the body as to make it necessary to view events in them through a number of fundamental medical disciplines.

Reduced to simplest terms, breathing originates in the respiratory center in the medulla. The metabolism of this collection of nervous tissues continuously produces carbon dioxide. When carbon dioxide reaches a certain concentration in this center, a series of impulses are discharged that result in inspiration. Since carbon dioxide is a substance that diffuses rapidly through a watery medium, it is to be expected that as it accumulates in the center it will also be diffusing out toward the blood. If one breathes a gas mixture containing 5 to 10 per cent carbon dioxide, the blood going through the respiratory center will contain more than the usual amount of the gas and outward diffusion will be slowed, which, in turn, will favor the more rapid attainment of discharge concentrations and a consequent increase in breathing.

One may believe that the discharge concentration for the center is not always the same. It depends on the setting or condition of the center at the moment, somewhat as one might expect to have to apply a hotter poker to a pile of damp

powder to explode it than would be necessary for dry powder. It is this setting of the center that is most important. There are few drugs that stimulate breathing, but there are many that depress it. Ether, alcohol and chloroform all depress breathing when they pass beyond their initial effects. Morphine is notable in this direction, and the barbiturates all produce a certain degree of anoxia in animals breathing air if they are given to the point of producing anesthesia. Far more important than any drug for its dampening effect on the respiratory center is lack of oxygen. By this is meant that essential automatic discharge of impulses by the center as a result of the accumulation of carbon dioxide is progressively hindered as anoxia develops. The increase in breathing following inhalation of 7 per cent carbon dioxide becomes less if it is repeatedly tested during anoxia produced slowly by means of carbon monoxide. It is quite true that in the carotid and aortic bodies chemoreceptors are present that are stimulated by oxygen lack, but the hyperpnea resulting from oxygen lack is a weak affair compared with what is obtained from carbon dioxide in the presence of normally ample oxygen. Furthermore, stimulation of breathing through oxygen lack is in many reactions similar to nerve stimulation. To be effective there must be a sudden rise in the intensity of the stimulus. Anoxia, as one usually sees it, develops insidiously and may become quite marked without noticeably disturbing the rate or volume of the breathing. In summary, so far as anoxia is concerned, the reactions of the central nervous system are not on the whole very serviceable against the progress of the condition. It is curious that evolution has not resulted in better protection by the central nervous system against oxygen lack, but the fact is that anoxia begets anoxia, an axiom too often forgotten in the management of patients.

If oxygen lack is accompanied by a gradual loss of efficiency in the central mechanism controlling breathing and thus by depreciation of the oxygen

*From the Department of Physiology, Harvard School of Public Health.

A lecture delivered at the Children's Hospital, Boston, on March 30, 1944.

†Professor of physiology, Harvard School of Public Health.

intake, its results on the smallest blood vessels are even more significant. It was Krogh's idea that anoxia is responsible for many localized dilations of capillaries. Lewis, a little later, concluded that as a result of anoxia, and of trauma of the most varied sorts, an "H substance" is formed locally and causes the reaction in question. This

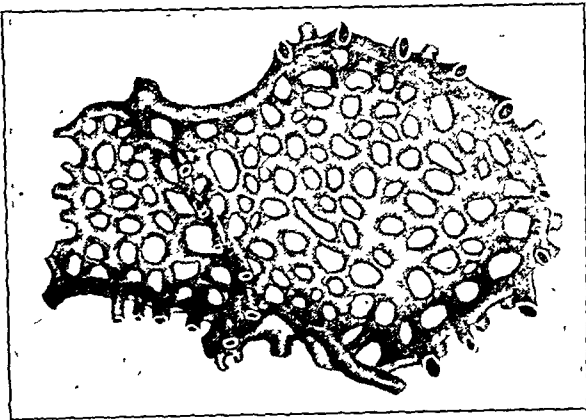


FIGURE 1. *Reconstruction of Capillaries in the Walls of Alveoli (x280) (reproduced from Miller by permission of the publisher).*
Note the absence of long capillaries. The total surface area for gas diffusion provided by this close net is estimated at 140 square meters in a normal adult.

idea, supported by a variety of ingenious experiments, induced many people to neglect Krogh's position. He considered lack of oxygen to be a special form of chemical injury, which caused capillary dilatation through formation of a variety of substances, not of a single histaminelike product. This conception is probably more nearly correct than the simpler one of Lewis and puts anoxia in the special position it deserves. I know of no exception to the fact that systemic capillaries in all parts of the body dilate as a result of oxygen lack. Some are less responsive than others, but the rule seems to be that when a tissue becomes anoxic the capillary bed becomes larger. In many cases dilatation is accompanied by increased permeability, so that edema also occurs, but in the experience of most investigators abnormal leakage is not an essential companion of larger capillary diameter unless the change is extreme.

Our concern today is with the lung capillaries. In spite of evidence purporting to show it, there is no reason to believe that these capillaries possess active powers of contraction and dilatation as is the case with practically all the systemic vessels. This does not mean that their diameter does not change, nor that at times there are capillaries that are not conducting blood and that may later be filled by a moving current. These changes are, I believe, passive and depend on variations in the output of the right ventricle or a rise in pressure in the pulmonary veins. The capillary net in the

lungs is for the purpose of gathering oxygen to serve the entire body and for eliminating all the carbon dioxide produced. The vessels lie in a tissue so delicate that it is structurally almost the foam the ancients believed it to be, and is at the same time highly elastic. The lungs must meet the needs of the body when the cardiac output is 4000 cc. a minute and when it rises abruptly even to 30,000 cc., and this result is best obtained if the vascular bed is large enough for the greatest needs, and so arranged as to give all parts of it a practically equal chance to receive increased amounts of blood instantly and without any adaptive opening reaction (Fig. 1).

That the lung capillaries do not dilate adaptively as a result of oxygen lack does not exclude them from the second effect of anoxia, — namely, increased permeability, — and anoxia does make these vessels leak abnormally, a fact all too apparent as one watches the slow progress of pulmonary edema or, perhaps even more frequently as one looks at the lungs at autopsy.

It is necessary to appreciate certain anatomical and physiologic facts and deductions about the lung capillaries. The situation to be examined is provided by a diagram (Fig. 2) constructed

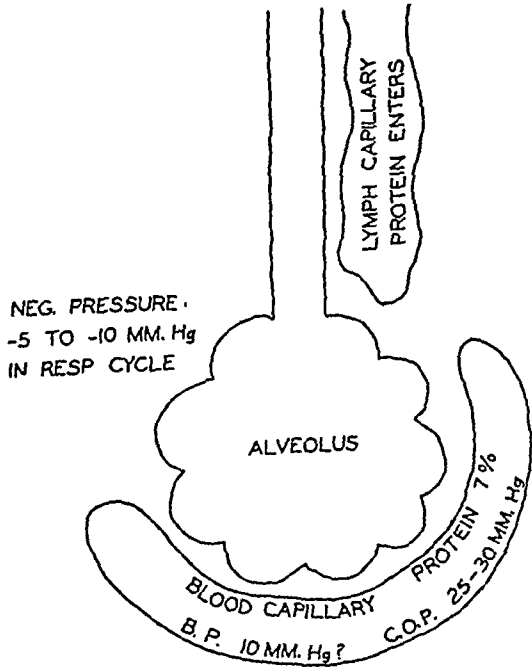


FIGURE 2. *Diagram of Certain Fundamental Conditions That Must Be Considered in Connection with the Formation and Removal of Pulmonary Transudates and Exudates.*

for the lungs on the basis of what is known to be operative in the case of systemic capillaries. In this diagram there is a capillary containing blood with a normal plasma protein content of 7 per cent, and this protein exerts an osmotic pressure — the colloid osmotic pressure of

asma of 25 to 30 mm. of mercury. In most systemic capillaries this force, which attracts water into the vessels, is opposed by the capillary blood pressure derived from the left ventricle and of about the same magnitude. There is thus a balance of forces that controls movements of water and dissolved salts through the capillary endothelium. In the lungs the colloid osmotic pressure drawing in water is necessarily 25 to 30 mm., but the opposing capillary blood pressure is not known. It must be low, and 10 mm. is a fair value. This means that in the lungs relative dryness of the tissue is substantially safeguarded and that under normal conditions extravascular fluid is in reality intracellular fluid. There are, however, local disturbers of this balance. The walls of the lung capillaries are separated from the alveolar air by a single layer of extremely thin epithelial cells. At each normal inspiration the pressure in the trachea becomes negative (-3 mm.), and this effect extends through the bronchi into the alveoli. At the end of inspiration, air having entered the alveoli as a result of atmospheric pressure, the intra-alveolar pressure becomes zero and rises slightly during expiration. This means that for outward filtration of water during inspiration an element of suction is added, and thus the filtering pressure is above 10 mm., and since a negative intrapulmonic pressure of 50 mm. may readily result from the obstruction of the trachea, it is clear that high filtering-out pressures may accompany half the respiratory cycle over long periods of time. It is true that the expiratory phase of breathing reverses the state of affairs, and that with the lung tissue wholly normal mechanical conditions that would result in the production of significant capillary leakage do not occur. But one must bear in mind that there is a single restraining influence for keeping water in the lung capillaries, which is fixed in the sense of being unalterable by local changes — the concentration of the blood proteins and their colloid osmotic pressure.

The other factors in the diagram are changed more or less readily, and all more readily in the direction of production of edema than against it. Thus, the permeability of the capillary endothelium may be increased by anoxia and by the action of drugs. The pressure in the lung capillaries is hard to disturb because of the immense area of the vascular net and the readiness with which expansion can be induced, but increases in pulmonary capillary pressure accompany cardiac disease, particularly while the right ventricle is still competent and a high-pressure head for outward filtration of fluid is maintained. This pressure may be enhanced by increased negative pressure in the alveoli during dyspnea. The human system depends for lung dryness on what Meltzer² years ago termed "a factor of safety" inherent in the predominance of osmotic retention of capillary water. This "safety"

is assailable from a number of directions, and the attack is never achieved by a single one of the assailing forces but practically always by many of them. Of the factors leading to edema, increased permeability of the lung capillaries is by far the most important and of all the possibilities for inducing it, anoxia is infinitely the most frequent.

There are two other items in the diagram that have not been mentioned. The first of these is the negative intrapleural pressure. Graham³ in 1921 expressed the belief that prolonged increase in the negative intrapleural pressure may suck fluid through the pleura and cause pleural effusion. This is true. Indeed, it has been shown that apparently normal men subjected to hard physical exercise accumulate pleural transudates. It is apparently the increased breathing of the exercise that does this, through the sucking action of lowered intrapleural pressure during vigorous inspiration.

The final component of the diagram is a lymphatic. Wherever lymphatics are found in the body their principal function is the carrying off of small amounts of protein that have left the blood capillaries. In addition to this regular function, the lymphatics take away other things in the tissues not readily absorbed by the blood vessels, among these being bacteria, foreign particles of many varieties and the detritus accompanying inflammation. The distribution of lymphatics is most profuse in parts of the body that are essentially surfaces between the interior of the body and the outside world. A well-known example is the extraordinary number and size of the lymph capillaries in the nasopharyngeal mucosa and in the mucosa of the female genital tract. In these regions, in addition to the constant possibility of infection, with the necessity of removing highly proteinized exudates, there are rhythmic periods of edema due to transudation of fluid containing much protein. The lungs seem to be free from any need to be constantly cleared of excess tissue fluid, but it is a fact that they are as profusely supplied with lymphatics as is practically any tissue in the body. Lymphatics are constantly seen in lung sections, but one has a poor idea of their number or extent and of their ability to rid the lungs of fluid. Over the surfaces of the arteries, veins and bronchi are lymph vessels, obviously large vessels. Their ends do not reach into the actual alveolar walls but stop as blind terminals in the walls of the alveolar ducts. An idea of the extent and capacity of the lung lymphatics is gained by a reconstruction of a typical plexus about a pulmonary vein (Fig. 3).

In spite of this profusion of lymph channels, it is puzzling to find that the arrangement for delivering their contents into the blood is curiously inadequate. The fact is that all the lymph from the lungs except a very small amount from the upper part of the left lung empties into the right sub-

clavian vein by way of the right lymphatic duct, which is usually a short tube not more than a millimeter in inside diameter. This vessel is an astonishingly small bottleneck at the delivery end of a large reservoir for accumulating proteinized and waste-containing fluid.

Let us now consider the bearing of these and other matters on asphyxia of the lung capillaries.

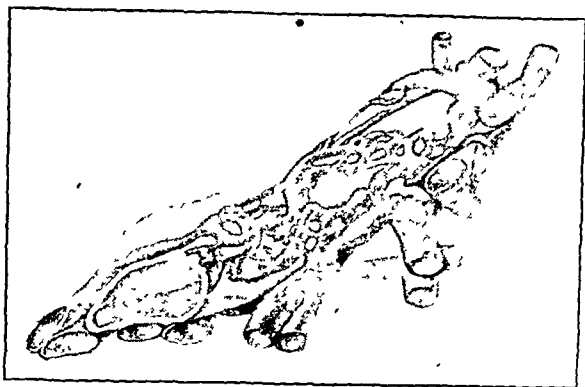


FIGURE 3. *Plexus of Lymphatics about a Pulmonary Vein (x15) (reproduced from Miller¹ by permission of the publisher). This particular vein was situated in an interlobular septum.*

Their endothelium is in the peculiar situation of receiving oxygen directly from the air, not at second hand from the blood. From the latter, all that the endothelium can gain is the precarious supply still remaining in the venous blood. This makes the lung capillaries dependent on the oxygen content of the alveoli in whose walls they lie. The body in general gets oxygen through the entire absorbing surface of the lungs, but the situation of the alveolar capillaries is not so safeguarded, and as transudation from these vessels begins they are steadily more and more widely separated from their oxygen supply.

To illustrate, there is employed a section of lung where exudate is forming and has formed (Fig. 4). One should observe the clear space under the pulmonary epithelium, which has been pushed loose in a continuous sheet. There is exudate in the alveolus, which may interfere with ventilation, and a layer of fluid under the epithelium and between it and the capillary wall. There are three possible ways of getting rid of this exudate. It may drift up through the air passages and be coughed out, may be broken down by enzymes and absorbed into the blood, or may drain off through the lymphatics. This last pathway is immediately available for interstitial exudate, which, as it accumulates in the alveolar wall, must eventually surround a capillary lymphatic terminal and enter it, to move slowly toward the right lymphatic duct through the enormous lymphatic network described, in every case traversing at least one lymph node. It is not surprising that when one causes continuous and copious leakage of lung capillaries, one finds bronchi

and blood vessels surrounded by rings of fluid. In such a case, as is illustrated in a low-power photomicrograph (Fig. 5), most of the thin-walled intercommunicating lymphatics have apparently been ruptured, and lymph drifts along the blood vessel as a grossly visible sleeve of dilute blood plasma, which may or may not reach the narrow neck of the funnel — the right lymphatic duct.

All this indicates clearly enough that the lung are not provided with any too adequate means of getting clear of exudates once they are present, and obviously exudates interfere profoundly with the entrance of air into alveoli and the passage of oxygen into lung capillaries. So in the lungs as well as in the respiratory center anoxia begets anoxia.

How vulnerable the lungs are to oxygen lack can be approximately shown by an example. If the lungs of a normal dog are ventilated artificially so that the mechanical factors in breathing are held constant and lymph is collected from the right lymphatic duct, the flow of lymph increases and the lymph becomes bloody when the oxygen in the air is reduced to 8.5 per cent; if one shifts back to 100 per cent oxygen, the flow soon falls to normal and the red cells disappear.⁴ It must be realized that this experiment has to be a rather crude one, carried out on a curarized animal under constant conditions of artificial respiration, which inflates the lungs through positive pressure and allows expiration to occur passively. Positive-pressure ventilation does not reach the alveoli

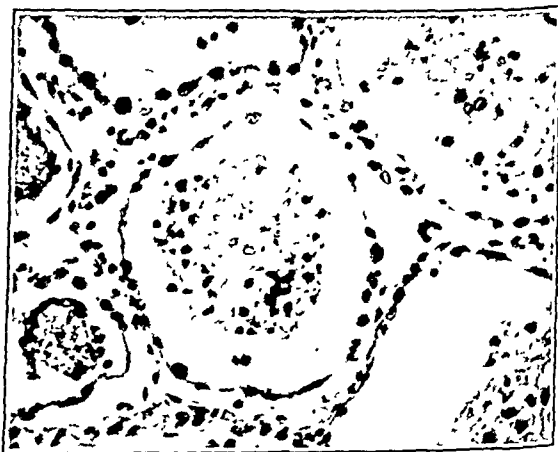


FIGURE 4. *Section of an Exudate-Containing Lung (x345) (reproduced from Miller¹ by permission of the publisher).*

The epithelium lining the alveolus in the center of the figure has been pushed off as a continuous sheet. Certain of the cells are more swollen than others. The alveolus in the upper right of the figure shows clearly the epithelium before and after an exudate has raised it from the surface of the alveolar wall.

throughout the lungs with anything like the efficiency of the negative-pressure ventilation of normal breathing. It is thus quite probable that the transudation reflected in the lymph comes from parts of the lung that are receiving little or none

of the oxygen-poor mixture employed, and that the capillary endothelium of the lungs is much more resistant to oxygen lack than the experiment indicates. But even if this is the case, it is obvious that parts of the lungs have been affected and that a return to adequate oxygen in the air is followed by prompt restoration to normal. If, however, the experiment is carried out more slowly and abnormal capillary leakage is continued for some time, restoration of normal conditions through the use of oxygen is greatly delayed or does not occur during the experiment. Furthermore, if the pressure in the lung capillaries is increased by tightening a clamp on

oxygen in 1914, when I entered the Peter Bent Brigham Hospital as a house officer, was negligible, but this entire lack of reliance on oxygen has given way to a better appreciation of what it can accomplish. The reasons why there is still too little use of oxygen are as follows. In the first place, anoxia is essentially progressive. If the physician begins to use oxygen when he is sure that it is needed, he has incurred a handicap that is usually insurmountable. The time to begin to use oxygen is before there is any certainty it is needed. Secondly, the present methods for administering oxygen are expensive and inefficient. It will probably be



FIGURE 5. Section of the Lung of a Dog with Severe Exudation ($\times 18$)
Note the rings of relatively clear fluid surrounding the blood vessels and bronchi.

the pulmonary veins when oxygen-poor air is used for ventilation, the lung lymph changes in a very short time into what is practically blood.

One may be deceived in regard to the onset of lung edema by the fact that the lungs are so much larger than the resting subject requires. If the process begins in a dependent part of a lobe and transudate travels up bronchi and obstructs neighboring bronchi, no attention is paid to it until the patient, at rest and so requiring the least possible oxygen, takes a distinct turn for the worse. When this happens, the lungs, as receiving structures, where gas exchange can occur readily, are greatly reduced in functional size and the safety inherent in their normal oversize is lost. The probability is that the condition will progress further, not only by local spread of excess fluid in the lungs but also because as anoxia increases the efficiency of the respiratory efforts often becomes less.

It is my task to speak of but one of the measures for combating anoxia. It is the obvious one — administration of oxygen. The therapeutic use of

a long time before oxygen therapy is inexpensive, but that is not of so much moment as is inefficiency.

Pure oxygen has five times the power to penetrate exudates and reach anoxic parts of the lungs and the blood going through them that air oxygen has. Pure oxygen breathed continuously for eight to twelve hours is of itself irritating to the respiratory passages, but minor interruptions from time to time are enough to dispose of this danger, which is not a potent one unless oxygen is breathed under a pressure of two to three atmospheres. Oxygen tents often do much for patients, but they are leaky, inefficient affairs in which the oxygen concentration is usually well below 60 per cent. Mask administration of oxygen has improved, and if the experience gained during the war is utilized it can be carried much farther. Lastly, there is a failure to realize the possible advantages to be gained even from poorly administered oxygen in many ordinary conditions. For example, there is no drug that gives such great subjective relief or such valuable rest in dyspnea as does morphine, but this drug dampens

clavian vein by way of the right lymphatic duct, which is usually a short tube not more than a millimeter in inside diameter. This vessel is an astonishingly small bottleneck at the delivery end of a large reservoir for accumulating proteinized and waste-containing fluid.

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many points of dissimilarity between the two diseases, which are sufficient to prove that they are separate though allied infections.

One of the striking differences between yaws and syphilis is that in yaws the infection is usually, if not always, extragenital. Again, in the secondary period there are no lesions of the mucous membranes, the absence of vaginal mucous patches probably accounting for the failure of infection by sexual intercourse. Another difference is the absence of intrauterine infection in yaws, there being no lesions in children that suggest congenital syphilis.

Yaws is a milder infection than syphilis because it does not affect to any appreciable extent the vital structure of the body. It is doubtful whether the viscera are affected by yaws, and lesions of the cardiovascular and central nervous systems are mild compared with those of syphilis. The statement is often made that no one seems to die of yaws, although in the late stages severe deformities may result from lesions of the skin, mucous membranes, bones, tendons and joints. The lessened tendency for yaws to attack the blood vessels is seen in histologic sections of cutaneous lesions. These do not show the same tendency as the lesions of syphilis to produce endarteritis. Yaws also yields to treatment more rapidly than does syphilis.

There are differences between the immune reactions of yaws and of syphilis, but eventually, at times after ten years, there is a complete cross immunity between the two diseases. This is well shown in the island of Guam, where most of the natives are immune to syphilis, since they have been infected as children with yaws.

PINTA

Pinta, like many other tropical diseases, has numerous local names. In Mexico, for example, it is called *mal del pinto*, in Colombia *carate* and in Venezuela *cute*. Pinta is an infectious disease mostly confined to the American tropics. It is caused by a treponema that is morphologically identical with the organism causing syphilis and yaws.

For many years the disease was thought to be due to a fungus, this theory persisting for eleven years after it was first shown that the serologic tests were positive in a large proportion of cases. By 1930, it was shown that the serologic reaction with both complement-fixation and flocculation tests in the pigmentary stage was almost 100 per cent positive. This was comparable to the serologic changes in syphilis and yaws. After the discovery of the causative treponema in 1937 by Armenteros and Grau Triana, the fungus theory was discarded.

The greatest incidence of pinta is found in Colombia and the southern half of the Republic of Mexico. A careful survey made a few years ago in Mexico disclosed the presence of over 270,000 cases. The

disease affects chiefly the dark-skinned races, including Indians, Negroes and those of mixed blood. It is rarely seen in Whites. This fact helps to substantiate the claim that the disease is caused by personal contact and not by the bite of an insect or other arthropod. At least there is no definite knowledge concerning a possible insect vector.

Soon after the discovery of the causative organism, Leon y Blanco went to Mexico and proved that the disease is inoculable in man and that syphilis gives no immunity to it. The same investigator showed that a primary scaly plaque represents the initial lesion, which is often followed by nondescript secondary lesions of the skin. Eventually, the pigmentary stage ensues and lasts for years or decades. Previous to the discovery of a possible primary and secondary stage, the pigmentary disturbances were thought to constitute the entire picture of pinta.

The pigmentary stage consists essentially of slaty-blue patches appearing especially on uncovered parts as freckles or diffuse areas. Eventually a partial depigmentation appears, and if untreated the process in some cases continues until the patches are completely devoid of pigment. The eruption is then indistinguishable from ordinary vitiligo and is a permanent defect, the normal pigment never returning.

The serologic reaction in pinta is positive in nearly 100 per cent of cases in only the late (pigmentary) stage, whereas in the primary stage it is negative and in the secondary stage, when recognized, is said to be positive in 60 per cent of cases. In this regard pinta differs from the other two treponematoses, syphilis and yaws, in which the strongest positive reactions occur in the secondary stage and gradually lessen in the late stages. As a rule, there are no abnormalities in the spinal fluid in pinta.

The typical slate-blue color is due to the large number of melanophores in the cutis and not, as was originally thought, to the action of fungi.

Pinta, in the vast majority of cases, is an essentially harmless disease, except for the cosmetic deformity, which in some cases is severe. Those who suffer from pinta are apparently able to work as hard as are others who are not affected with the disease.

CUTANEOUS LEISHMANIASIS

Cutaneous leishmaniasis may be divided into the type seen in parts of the Old World and known as Oriental sore, Aleppo boil, Biskra button and so forth and the type appearing in the Western Hemisphere, known as American or mucocutaneous leishmaniasis. Both these types are caused by parasites, called "leishmaniae" in honor of Colonel Sir William Leishman, who first discovered them in kala-azar. The parasites causing the two types are morphologically indistinguishable in microscopic preparations made from scrapings and in cultures.

the respiratory center and thus promotes anoxia. There is no reason why the use of oxygen with morphine should not allow all possible benefit from the sedative without the progression of anoxia. Similarly, after operations, particularly in elderly patients with fairly rigid chests and pain on breathing that still further restricts respiratory movement, oxygen therapy may for a time permit the economy of lung movement that the patient involuntarily provides, and the use of a much needed sedative may be robbed of some of its danger.

It would be possible to multiply such illustrations indefinitely. These are enough, and they, with all that has been said above, may help to enforce further

the two principles that the laboratory has learned: the master words in oxygen therapy: anoxia begs oxygen, and if real benefit is to be expected from oxygen, it should be used before the need is certain.

55 Shattuck Street

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TROPICAL DISEASES OF THE SKIN*

HOWARD FOX, M.D.†

NEW YORK CITY

IN THIS paper will be discussed five diseases in which cutaneous manifestations constitute either the whole clinical picture or an important part of it. Three of these diseases, yaws, pinta and verruga peruana, are almost entirely confined to the tropics, and the other two, cutaneous leishmaniasis and leprosy, are at least more prevalent in tropical than in temperate climates.

The present interest in tropical diseases is mainly due to the possibility of their being contracted by the members of our armed forces. Of the diseases in question, the likeliest ones to affect our soldiers and sailors are cutaneous leishmaniasis and leprosy. It is almost certain that a few men at least will contract these diseases, although in the case of leprosy there may be no active manifestations for a number of years after their return to the United States. Information about tropical diseases of the skin will also be of value to medical officers whose duty it may be to take care of native populations, both during and perhaps for some time after the war.

YAWS

Yaws (*frambesia tropica*) is an infectious disease caused by *Treponema pertenue*, an organism that is morphologically identical with *T. pallidum*. The disease occurs almost exclusively in dark-skinned races, especially Negroes. The fact that the white man rarely suffers from yaws is probably due to personal hygiene and not to any racial immunity. The geographic distribution of yaws is widespread and includes parts of equatorial Africa, many islands of the Pacific, Burma, Thailand, some islands of

the West Indies and tropical parts of South America. The disease is contracted most often in childhood usually by personal contact, although in some cases the infection is transmitted directly by certain flies. The initial lesion or so-called "mother yaw" may not be observed. It does not remotely resemble the chancre of syphilis, and is merely the largest lesion of the type of the ordinary secondary or frambesiform eruption.

The typical eruption of yaws — frambesiform — begins as small papules that tend to coalesce, soften and discharge a fluid that forms typical amber-colored crusts. It does not resemble any ordinary eruption of syphilis but rather suggests an impetigo. The eruption lasts for months up to a year or two and disappears spontaneously without leaving any permanent trace. Another characteristic eruption is a hyperkeratosis of the soles, called "crab yaws" by the natives of the West Indies. The term is used because the affected persons walk like a crab, owing to soreness caused by secondary infection. The eruption is not due merely to walking barefoot, since barefooted natives who suffer from syphilis do not often present this characteristic eruption.

There are two frequent manifestations of early syphilis that have never been observed in yaws. They are iritis — or iridocyclitis — and alopecia, including both a diffuse thinning of the hair and the patchy so-called "moth-eaten" type so characteristic of syphilis.

There are four features that yaws and syphilis have in common. In both diseases the causative organisms are morphologically identical, both of them give the same serologic reactions, both yield to arsenamine and allied drugs and to bismuth, and in both the late destructive tertiary lesions are clinically indistinguishable. There are, however,

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†Professor emeritus of dermatology and syphilology, New York University School of Medicine.

Oroya fever is a most serious disease, with an average mortality of about 40 per cent, and presents the symptoms of pernicious anemia, with a sudden and tremendous drop in the red-cell count. *Veruga peruana*, after the stage of incubation, is also accompanied by febrile symptoms and anemia, but the latter is of the simple type. After a period of several months, an eruption appears and the patient is then on the road to recovery. The eruption is a unique one and consists of lesions that resemble pyogenic granulomas, senile angiomas or a general sarcomatosis. The eruption disappears spontaneously in a few months, and the patient is thereafter immune.

The causative organism is seen in the red cells of the peripheral blood in varying numbers (from one to ten or more). In culture it appears as rod-like bodies or as cocci.

The vector was proved to be night-flying species of *Phlebotomus*, whose habitat corresponds exactly to the areas where the disease is contracted. This is in deep ravines at an altitude between 2800 and 9000 feet. Most of the inhabitants of these ravines contract the disease in infancy or early childhood, when it causes only mild symptoms. There is no known specific treatment. Prophylaxis is all important. Townsend states that no one ever contracts the disease in Peru unless he has spent one or more nights in the infected ravines.

LEPROSY

Leprosy is a serious disease that carries an undeserved stigma. This is partly due to the Biblical descriptions of a disease that was in all probability the same as the one now called leprosy. The disease has a world-wide distribution; although it exists in cold and temperate climates, its greatest incidence is in the tropics. It has been roughly estimated that there are 3,000,000 lepers in the world, about 30,000 of whom are in the Western Hemisphere. In the United States, it is estimated that there are 1000 or more cases, and in New York City there are always 25 or more cases known to the health authorities. All the latter are imported cases.

Contrary to popular belief, leprosy is not highly contagious. To contract the disease it is usually

necessary to be exposed to it for long periods, especially in hot and humid regions. The method of transmission is not known, although infection of the nasal mucosa by the fingers is thought in many cases to be the cause. The disease is apparently not contracted by sexual intercourse.

Leprosy affects all races and both sexes and is oftenest contracted in the fifth to the twentieth year of life. The disease is neither congenital nor hereditary. It is undoubtedly caused by *Mycobacterium leprae* (Hansen's bacillus), even though the postulates of Koch have not been fulfilled. The disease is strictly confined to man and does not affect any of the lower animals.

The terminology of leprosy lesions has been the source of considerable confusion. At the present time, one speaks of the two essentially different types as lepromatous, — formerly called nodular, — and neural, which can be subdivided into pure neural, maculoanesthetic and tuberculoid. The neural type has the signs and symptoms of a peripheral neuritis, the disease not affecting the brain or spinal cord. The neural type is the one oftener seen in the tropics and is decidedly more favorable in prognosis than the lepromatous type. It may cause severe mutilations, but the disease may become arrested and the patient live for decades thereafter.

One of the numerous problems to be settled in the future is why the disease is transmissible in some regions and not in others. For instance, Louisiana, Texas and Florida are now practically the only endemic centers in the United States. On the other hand, although there are always lepers in New York City, there is no case on record in which a person has contracted the disease in or near this city. In every case the person has spent more or less time in a part of the world where the disease is endemic. It therefore seems eminently proper to allow lepers in New York City to go at large, although they must report at intervals to the local health authorities.

The only way to eradicate leprosy is by segregation. In my opinion, there is as yet no specific remedy for the disease.

140 East 54th Street

Oriental sore has a widespread geographic location, including Africa, Asia and parts of Europe. In Africa it occurs along the Mediterranean coast. In Asia Minor it is especially rife in Syria, Palestine and Armenia. It is endemic in the southern and eastern parts of Asia, and in Europe it occurs in Greece, Italy, Sicily, Cypress and Crete. This incomplete list shows numerous areas in which our armed forces are exposed to this disease.

Oriental sore may be contracted either by the bite of some species of sandfly (*Phlebotomus*) or by personal contact, as from one child to another. The disease is also occasionally transmitted by the common housefly. In certain areas dogs are infected, especially about the snout, and constitute a reservoir for the parasites.

The incubation period of Oriental sore varies from a few weeks to many months or at times a year. The eruption begins as small papules that enlarge and form a buttonlike plaque several centimeters in diameter. Eventually it becomes an ulcer covered with adherent crusts. It does not suggest the appearance of a boil, and the term "Aleppo boil" is therefore a misnomer. Healing is usually followed by scars, which may be disfiguring. There may be a single lesion or several, as many as a hundred or more having been observed.

Oriental sore is usually confined to the skin and as a rule occurs on the uncovered parts of the body. In the vast majority of cases it heals within a year as the Turkish name *habel-seneh* ("button of one year") indicates. In rare cases the disease lasts for many years. As a rule, when the eruption clears spontaneously or from treatment it is followed by permanent immunity. In extremely rare cases there is a recurrence. The disease is purely a local one and causes no constitutional symptoms.

The eruption must at times be differentiated from that of syphilis, tuberculosis, blastomycosis, ecthyma, bromoderma and tropical and other ulcers. An unquestioned diagnosis depends on finding the parasites in smear preparations—stained by Wright's method—or in cultures. In difficult cases, help has been given by intracutaneous tests of material from killed parasites.

Innumerable methods of treatment have been tried, with varying success. Excellent results have been obtained with x-rays and grenz rays, which, however, are not generally available. Care must be used with escharotics, since the disease is not a serious one and constitutes only a cosmetic defect. *Excellent results have been claimed by freezing with man rarely suffers from it.* Prophylactic treatment in personal hygiene and in the use of insect repellents. The geographic distribution with forty-five holes to and includes parts of equatorial and subequatorial regions of the Pacific, Burma, Thailand, *leishmaniasis*

Peninsula. The disease in the majority of cases is an occupational one, and is seen most often among foresters in Brazil, workers on tea plantations in Paraguay and chicle pickers in Guatemala and Yucatan. It is probably caused as a rule by the bite of some species of *Phlebotomus*, although infection by personal contact is possible. The causative organism is identical in appearance with that of the other types of leishmaniasis.

The American type differs from Oriental sore in its tendency to last for years and to attack the mucous membranes of the nose and throat, as it does in 15 to 20 per cent of cases.

The cutaneous lesions consist of one or more ulcers, occasionally a hundred or more. At first glance they appear to be nondescript, but they usually have a halo that is red and edematous. Lesions of the nose and throat, if present, usually follow cutaneous lesions by years and may be extremely deforming.

Treatment of cutaneous lesions by tartar emetic gives satisfactory results, but this remedy is not so efficient for lesions of the mucous membranes.

VERRUGA PERUANA

Verruga peruana (bartonellosis) is now known to be one phase—the other being Oroya fever—of a disease that has probably existed in Peru for centuries. It has recently been observed in both Colombia and Ecuador.

Little was known of *verruca peruana* until 1870, when a railroad was built over the Andes. A violent epidemic resulted in which 7000 laborers died and 100 American and British engineers contracted the disease, half of them dying of it. In 1885, a brilliant young Peruvian medical student allowed himself to be inoculated with the harmless *verruca peruana* and died of severe Oroya fever. This convinced the Peruvian physicians that the two types probably represented the same disease. In 1913, Strong and others forming a commission from Harvard University visited Peru and concluded erroneously that *verruca peruana* and Oroya fever were separate diseases. In 1909, the causative organism, which is now thought to be a rickettsia, was discovered by Barton and was successfully cultured in 1926 by Noguchi and Battistini. Monkeys were inoculated by Noguchi with a culture from a case of Oroya fever and *verruca peruana* resulted. A year later, Mayer and Kikuth in Hamburg inoculated monkeys from a case of *verruca* and produced fatal Oroya fever. There was also a physician in Lima who accidentally inoculated his finger while giving a transfusion to a patient dying of Oroya fever. Fortunately he developed *verruca peruana* of the harmless type and recovered. From these facts it seems clear that *verruca peruana* and Oroya fever are different phases of the same disease.

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

†Professor emeritus of dermatology and syphilology, Harvard Medical School.

misuse of the Snellen test in the public schools of Massachusetts since 1906 are illuminating:

Teachers, having to rely on an instruction sheet that is furnished with the chart to guide them, often failed to observe one or more fundamental requirements, such as making sure that the eye not being tested was covered, or that the chart was placed where illumination would be adequate, and without glare from reflected light.

Letter charts were used, which children committed to memory.

The use of letters precluded the vision testing of kindergarten and first-grade and second-grade children, most of whom were, for the purposes of the test, illiterate.

The experience gained by school authorities during the first few years suggested the need of measuring the vision of younger children. They appealed to the State Department of Education, which in turn requested the Department of Public Health to recommend a test chart for illiterates. A subcommittee of the Council on Public Health, made up of Drs. David L. Edsall and William J. Gallivan, in 1915 recommended a chart (Fig. 1) for the use of teachers testing illiterates, which since 1917 has been distributed on request to the schools of the Commonwealth. This chart,

BOSTON TEST CHART

50 FEET



40 FEET



30 FEET



20 FEET



FIGURE 1.

The Boston Test Chart differs from other standard charts in that symbols on the 30 and 20 foot lines are spaced more than 5 minutes apart.

which is based on the Snellen scale, was partly devised by Snellen himself¹ as a test for illiterates, using three parallel lines. Pergens² later joined these

lines on one side by a line of equal width. This is the most practical test object for use in schools, and moreover its use should not be limited to illiterates. It has three outstanding features. Firstly, after a short drill, conducted as a game, the vision of



FIGURE 2. Old Method of Occlusion.

This method, although dependable, required an extra teacher.

children over two years of age may be accurately tested with it. Secondly, it is not to be compared with capital letters, which when made as uniform as possible are visible from different distances.³ It therefore conforms more nearly than do other objects to the physiologic requirements for a test object. Finally, if the symbols are selected by the teacher conducting the test, as I⁴ have recommended, even a small chart, such as that furnished by the State Department of Education becomes unlearnable.

A test chart that can accomplish so many things faithfully is no mean device. Competent ophthalmologists during the last quarter of a century have filled many pages of printed matter with a variety of unique test symbols, all carefully drawn to the Snellen scale, but none of these, so far as I know, compare with the Pergens symbol. As for some ludicrous and impractical technics suggested to prevent school children from memorizing test letters, the least said of them the better.

In a previous paper, I⁴ suggested a technic for testing vision of school children. It required two

THE GOAL OF AN EYE-HYGIENE PROGRAM FOR SCHOOL CHILDREN*

JAMES J. REGAN, M.D.†

BOSTON

THE title of this paper implies that there should be some sort of program directed toward the maintenance of eye health in all schools. Such a program need not be expensive, requiring equipment, personnel and time, nor so extensive as to include a complete eye examination by a competent ophthalmologist, let us say three or four times during the child's school life. Its object is best expressed as a consciousness on the part of school administrators, teachers and pupils alike of the value of normal, comfortable vision to progress in health and education, coupled with a desire for positive action. It can take such form as facilities available in the locality permit and the support of the local school authorities provide. The program may range from tried and true yet simple procedures, such as annual medical inspection and tests of visual acuity for distance (the Snellen test), to the complete and periodic examination of each child by a competent ophthalmologist. It may be extended to include psychophysiologic studies of certain groups of children such as those presenting symptoms of reading disability—formerly referred to as congenital word blindness. It may include provision for instruction concerning the care of the eyes (personal hygiene) and accident prevention, and may stress the importance of paying more attention to the eyes during the routine medical inspection. It may furnish special educational facilities for the visually handicapped child. It may provide for better school buildings, artificial illumination, desks, printing of schoolbooks, as well as other printed and mimeographed material, window shades and wall paint. It may provide for good blackboards, properly located and cared for, to ensure maximum contrast and a minimum of glare from reflected light, and proper chalk, and may even place minimum limits on the size of letters and figures to be written on the blackboards.

Such a program may be expanded or contracted from year to year, reflecting any new advances in the fields of education, psychology, ophthalmology, architecture and engineering, and would survive curtailment of the school budget. It would even permit, occasionally, trial of newer technics of unproved value, without being seriously or permanently affected.

The consciousness of the value of good vision, which is the cornerstone of the program, must be

laid in teacher-training institutions. All elementary-grade and intermediate-grade teachers should have some knowledge of visual psychology, as well as of ophthalmologic anatomy, physiology and hygiene. They should be instructed in objective and subjective signs of eyestrain, and should be so well versed in a dependable vision-testing technic that their findings will be accurate. Because the teacher has the unique opportunity of observing the child at work every hour of the school day throughout the school year, any eye-hygiene program that does not include the teacher will fall far short of its goal. There is a mutual benefit to be derived. A child who sees well and comfortably is less of a drain on the teacher's time and patience than the child with poor vision.

Historically, it is true that teachers, rather than physicians, were responsible for the enactment of legislation in Massachusetts that, since 1906, has required that every child in the public schools have a vision and hearing test at the beginning of each school year, and that the class teacher conduct the tests. The prescribed vision test is one designed to measure the acuteness of distant vision, and nothing more. Admitting that it would be better to know more than is now known about the visual efficiency of school children, I am certain that it is wrong for any individual or group to challenge the value of the results of the Snellen test, provided that it is properly conducted. This test is simple and reliable, and involves no expense; it takes a minimum of school time; it requires no special equipment, eliminating such factors as cost, transportation, breakage and replacement; and it brings about the discovery of about 85 per cent of children with visual and other eye defects. It might, indeed, discover 10 per cent more, if it were supplemented by a simple test for detecting farsighted children, who have normal distant vision but find near work difficult. For these reasons, the value of such a test should be defended against attacks by groups, many of whom have equipment to sell and who, in order to impress school authorities with the superiority of their devices for discovering rare and usually unsymptomatic conditions, such as extraocular muscle imbalance, suppression or alternate fixation, poor stereopsis and astigmatism, feel obliged to declare the Snellen test worthless and the school system that uses it archaic.

The test is absolutely dependable, but educational authorities seem to have little regard for the valuable information it furnishes, and consequently bother little about the manner in which it is conducted. The following examples of the

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

†Assistant professor of ophthalmology, Tufts College Medical School; assistant in ophthalmology, Courses for Graduates, Harvard Medical School; ophthalmic surgeon-in-chief, Boston City Hospital; school physician, assigned to ophthalmologic duties, Boston Public Schools.

ads only to the third row, it is recorded as 20/30; only to the second row, as 20/40; and if only the top row, as 20/50. He should be made to read at least two symbols on the lowest row that he can see in order to get credit for the row. If he cannot see the top row, he should be told to approach the chart — always with one eye covered — and stop where he can see two symbols on the top row. If, for example, he walks to within 5 feet of the chart, his vision is recorded as 5/50.

FOLLOW-UP

Obviously, much of the time spent by school physicians and nurses in inspecting children's eyes and by teachers in testing their vision would be wasted

To recapitulate, the cornerstone of a workable, effective eye-hygiene program for school children rests on the development of a consciousness within the school system, especially among the teachers and pupils, of the value of normal vision to the progress of health and education. This may be developed through an educational program in the schools, sponsored by a joint committee of the State Department of Public Health and Department of Education. The committee's function should be to stimulate surveys by the school authorities in cities and towns throughout the Commonwealth. Interest might be created by first presenting to the heads of all school departments a copy of the statute requiring an annual vision

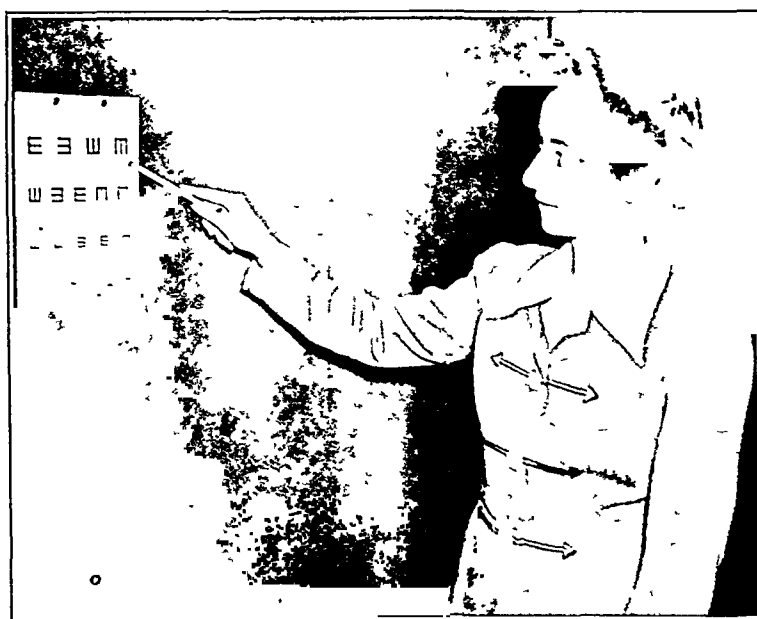


FIGURE 5. Method of Using the Test Chart.
The pointer should not mark the chart or cover any part of the symbol.

if some provision were not made by the school to follow up cases of defective vision and other eye conditions discovered or suspected, soon after a notice has been sent to the parent or guardian. Expert medical advice is available in normal times to school children of all economic groups in the large cities; in small towns and in rural communities, this presents a problem. The optometrist may be the only person available to provide eye care of any sort, but this service, even though limited in scope, may suffice for a large percentage of children with refractive errors, especially myopes. The more complicated cases should be brought to the nearest ophthalmologist or eye clinic by the parent, the school nurse or some other designated person. The disposition of indigent cases should be the concern of the school principal or physician.

* * *

test, together with an authoritative statement regarding the importance of conducting the tests properly, as well as obtaining relief for children early in the school year for those found defective.

With this accomplished, such a committee might arrange an outline for teachers, giving symptoms of eyestrain that may warrant a medical eye examination. Often a child with 20/20 vision in each eye suffers from sties, crusted red lids, watery eyes, irritated eyes or headache, especially after doing close work. Many of these children are farsighted, and if their accommodation is good, the Snellen test will not screen them out, but they suffer from and dislike close work, and are frequently truants. The committee might suggest a simple test for screening out this type of child at the time of the annual

teachers to conduct it, because the occluder used was a card measuring 3 by 5 inches (Fig. 2), and if the children were allowed to hold it and the better

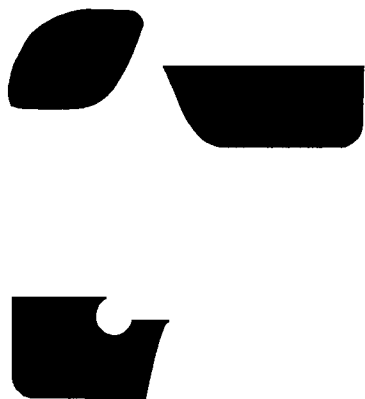


FIGURE 3. *Types of Occluders Used by the United States Navy. The newer form (above) permits observation of squinters and prevents artificial reduction of the size of the pupil by looking along the edge of the opening.*

eye was occluded, most of them peeked. The technic has been modified by substituting the more efficient occluder used by the Medical Department of the United States Navy (Fig. 3).

TECHNIC OF TESTING

The chart should be hung on an easel, black-board or other device, near a window (but not in direct sunlight) and at right angles to it; it may be hung in the window casing. If one end of the room is brighter than the other, the chart should be placed at the brighter end. Its height should be about the level of the average child's head. If there is glare* from windows between the chart and the child, the lower half of the window may be covered or the shade drawn. This is rarely an obstacle unless the child, standing at the 20-foot line, is abreast of a window.

A distance of exactly 20 feet should be measured from the chart along the windowed wall, a thumb-tack or chalk mark being placed on the floor or wall every 5 feet.

The occluder may be made of heavy cardboard, plastic or Masonite. The latter two materials are washable, even in antiseptics (a 1:1000 aqueous solution of Zephiran Chloride may be used). The occluder is held in the left hand with the opening in front of the right eye, which should always be tested first (Fig. 4). If the child wears glasses, he should be asked whether his vision is better with or without them. If it is better with glasses, the test should be made with them on, a notation to that effect being made on the record. If the vision is better without glasses, the test is made with them off.

*Glare is a brightness within the field of vision of such excessive character as to cause discomfort or interfere with vision

The record will be more complete if the vision is tested both with and without glasses, in which case the vision of the naked eye is tested first. (If the vision is better without glasses, it should not be concluded that they are not correct; instead, re-examination should be advised, especially if the glasses are more than a year old.) After the right eye has been tested, the child holds the occluder in the right hand with the opening in front of the left eye, and that eye is tested.

When pointing to the symbols the examiner should not stand on the window side of the chart, lest a shadow be cast upon it (Fig. 5). The point of a pencil should not be used, since it may mark the card. The pointer must not cover any part of the symbol. A symbol on the top row is selected, and the child is told to semaphore the direction in which the arms of the symbol point. If his direction is correct, a symbol is selected on the second row. If the child's answer is correct, one on the third row is chosen. If the direction is correct, at least two symbols on the fourth row are selected, one with its arms pointing up or down, and the other with its arms pointing to the left or right. One must



FIGURE 4. *Method of Using the Occluder.*

glance at the child frequently to see that the occluder is kept in place, as well as to see that he semaphores correctly.

If the child reads two or more symbols on the fourth row, the vision is recorded as 20/20. If he

MEDICAL PROGRESS

PHYSIOLOGY*

HEBBEL E. HOFF, M.D.†

MONTREAL, CANADA

THE last days of 1944 will bring a centenary as significant to physiologists and to all those whose concern is with experimental medicine as it is to surgeons and obstetricians. On the morning of December 11, 1844, Horace Wells, a dentist of Hartford, Connecticut, noticed the insensitivity to pain produced by nitrous oxide gas administered to Samuel Cooley by C. Q. Colton at a private exhibition, which followed a public lecture and a demonstration of "laughing gas" held the night before. Acutely conscious of the problem of pain in dental operations, because of the multiple extractions necessitated by an improved dental plate that he and W. G. Morton had devised somewhat earlier, Wells at once foresaw the practical application of the phenomenon he had witnessed. Enlisting Colton's aid, he returned to his office, where he inhaled the gas himself, while a fellow dentist removed a tooth that had been bothering him. Wells's subsequent efforts to introduce nitrous oxide as an anesthetic agent failed, and it was not until thirty years had passed that Colton, ever mindful of what he had seen in Hartford, persuaded another dentist to give public trial to the method, this time successfully. Wells's discovery nevertheless retains stature in the history of anesthesia, not only in the matter of priority as the second in the series of Long, Wells and Morton, but because of the intimate background this work forms to that of Morton, which introduced anesthesia to the world. Although in surgery equal honors are shared by asepsis and anesthesia, the former plays a lesser role in physiology, particularly in acute experiments and in species whose resistance to wound infection surpasses that of man. Anesthesia is, in truth, the cornerstone of physiologic technic, and the development of experimental medicine has been fostered in no insignificant way by the discovery that is shortly to be celebrated.

NITROGEN BALANCE IN STATES OF DAMAGE

In the progress report on physiology for 1941,¹ significance was seen in reports stressing the importance of high-protein diets in circumstances likely to be complicated by liver damage. Since then the subject of high-protein diets has attained a position as one of the most prominent factors in the care of patients suffering from infections, fractures

or burns, and in fact from almost any condition that inflicts damage on the organism.

The protein requirement of everyday life has not lacked attention, and it is generally assumed that for the average adult a daily intake of 1 gm. of protein per kilogram of body weight² is adequate. This may be reduced to 0.5 to 0.7 gm. in the presence of a high intake of carbohydrate and fat,³ owing to their protein-sparing activity. During pregnancy the protein intake may be increased by a half, and during lactation it should be two and a half times the usual amount.² Infants require no less than 4 gm. of protein per kilogram of body weight, and even at six years of age 2 to 3 gm. must be supplied.⁴

The increased protein requirements in typhoid fever have been recognized since 1909, and the work of Whipple demonstrated the importance of increased protein intake for the regeneration of hemoglobin during recovery from anemias. Peters and Bulger⁵ called attention to the fallacy of restricting the intake of protein in the nephritic syndrome, and demonstrated that patients losing albumin through diseased kidneys were often seriously depleted of protein, and required as long as three months to restore their protein stores when placed on a more adequate diet.

The more recent developments in this field come from two sources: the recognition by surgeons of the importance of an adequate protein intake in promoting adequate wound healing and the discovery of important protein loss in the early days following trauma—the so-called "toxic protein loss." The first phase no doubt stems from the work of Clark⁶ in 1919 on the influence of diet on the healing of wounds. He noticed that in dogs fed a fat-rich and protein-poor diet a period of quiescence occurred on suture of an experimental incision, which postponed by six days the beginning of healing and eventual recovery. Healing began at once in dogs fed a high-protein diet, shortening the time for full recovery by six days. Revived by Ravdin and his collaborators,⁶ the work of Clark has been fully substantiated, and Koster and Kasman⁷ have shown that the average concentration of plasma proteins in 40 cases of wound disruption was significantly lower than it was in 40 control cases of well-healed wounds. Difficulties due to a low intake of protein appear to be most serious in patients suffering from gastrointestinal disorders requiring surgery. This is partly because these patients have voluntarily

*From the Department of Physiology, McGill University

†Professor of physiology, McGill University.

vision test, even though this is not required by law.*⁵ Such children often require glasses for near work only, and may even leave them in school. It is of historical interest that Dr. Henry Willard Williams, first ophthalmic surgeon to the Boston City Hospital, presented a paper to the railroad surgeons of America in Chicago shortly after the Civil War in which he suggested this as a disqualifying test for railroad employees.

Such a committee could encourage the inclusion of some simple color-perception test, especially for junior-high-school pupils, who might be planning a career in art, aviation, the Navy or the textile industry. A few pieces of colored yarn or a half-dozen colored pencils would suffice to detect the color blind. The best approach to this group might be made through the Department of Vocational Guidance.

This work can progress to the study of regressive reading habits, heterophoria and stereopsis and to

*The simplest test for this purpose is one of a battery of tests known as the Massachusetts test, developed by Oak and Sloane.⁵ It is accomplished by placing a pair of spectacles containing plus spheres (+1.50 or +2.00) before the eyes of a child who has 20/20 vision. If he can still read 20/20, his farsightedness may well cause symptoms, either ocular or systemic, and reference for an eye examination is advisable.

the gaining of other information that may be of importance in promoting normal educational progress. But before any of these are undertaken, the important thing is to find out whether every school child has normal vision. With this work well done we shall be better qualified to evaluate properly the new lighting fixtures, optical aids and ophthalmic correctional devices so highly publicized. In this way a goal may be reached that is worthy of the American medical and educational tradition.

I am indebted to Lieutenant Commander E. H. Danis (MC), U.S.N.R., for calling the most recent type of Naocluder to my attention.

520 Commonwealth Avenue

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Correction. In the article "Pain and Disability of Shoulder and Arm Due to Herniation of the Nucleus Pulposus of Cervical Intervertebral Disks" by Drs. J. J. Michelsen and W. J. Mixter, which appeared in the August 24, 1944, issue of the *Journal*, the sublegend of Figure 2 should read as follows: "The three types are as follows: 1—herniation producing unilateral compression of the roots; 2—herniation producing unilateral compression of the ventral cord (Stookey's Group II); and 3—herniation producing bilateral compression of the ventral cord (Stookey's Group I)."

MEDICAL

protein in-calorie diet.
 PH₂ in and 3500
 protein daily
 HEP serious burns.⁴

AN

the past directed atten-

THE last days of 1944 will bring an adequate supply of significant to physiologists dramatic incidents in the one concern is with experimentsight the problem before the surgeons and obstetricia manner. In professional and December 11, 1844, Hor^a variety of measures have been rtford, Connecticut, ne-hirst at sea, including the juice in produced by nitrous can be expressed from fish, and muel Cooley by C. (er. A number of valuable research ition, which follow en in response to this problem, and monstration of "k₂ ning to appear in unrestricted pub-fore. Acutely con, ace,²⁹ who made studies of water ntal operations, volunteers who spent the greater part and W. G. Mor^{ly}. The weather conditions were such ells at once for ter requirement might be expected to ie phenomene e maximum to be found on any ocean. olton's aid, he ater loss by evaporation was calculated aled the gas hi a day, and it was estimated that so long tooth that h¹ is kept to a minimum, clothing is kept equent effort sea water and a light breeze blows, a nesthetic age 500 to 1000 cc. of water a day will prevent ie had pa rence of dehydration in semifasting sur-e had seen lifeboats and rafts in the tropics. Drink-o give publi r in these experiments was supplied by ully. Well- n which the salt in sea water is chemically n the histo ted.

of priority experiments have covered the effects on the and Morⁿ of varying degrees of dehydration. Earlier ground th by Collier and Maddock³⁰ indicated that introduce signs of dehydration begin when about 6 surgery it of the body's weight in water is lost. If anesthesi lost without excessive sweating, sodium and ology, He accumulate in the extracellular fluid of the species w In dogs deprived of water and food, loss of that of n and chloride is reduced practically to zero of phys gh the failure of the kidneys to excrete these perimer ances.³¹ The burro, an animal acclimatized to signific vironment of great heat, is said to sweat almost be cele water, and even man guards against excessive NITR of salt by reducing the amount of this substance rolonged sweating.³¹ The net result of this In less is a growing hypertonicity of the extra-signifi lar fluids, including the plasma. Concentrations portatigh as 186 milliequiv. of sodium and 133 millil-likely v. of chloride per liter of serum have been the ad in the dehydrated dog.³² Positlosely associated with the hypertonicity of the care- extracellular fluid of the body is an extra excretion potassium — that is, one unassociated with nitro-³³ loss — in the urine.³³ This can only mean that tassium has moved out of the cell, along with cell

water, and that this process mitigates the loss of extracellular fluid. Renal activity is essential for the process, for in animals with ligation of the ureters the phenomenon does not occur. Apparently, loss of potassium in excess of that derived from breakdown of tissue takes place in a number of circumstances in which the volume of extracellular fluid is reduced or the fluid in this compartment is hypertonic. Among the first to note the phenomenon were Gamble, Ross and Tisdall,³⁴ who detected it in fasting diabetic children, and concluded that it indicates dehydration of intracellular fluid as well as extracellular water loss. In diarrheal disease in children, Butler, McKhann and Gamble³⁵ noted that intracellular water was lost in quantities greater than was extracellular water. Atchley, Loeb and their co-workers³⁶ noted an increased potassium excretion during glycosuria or acidosis in diabetics, indicating that intracellular fluid participates in the dehydration developing in this condition. Excess potassium loss occurred even when sodium chloride was added to the dietary of salt-deficient animals,³⁷ and when dogs were bled to an extent of 2.0 to 3.5 per cent of their body weight.³⁸ These authors commented:

We are accustomed to regard interstitial fluid as an extensive reservoir from which plasma losses can be readily replaced, its electrolyte composition being so nearly identical with that of the plasma. That water and the unsuitable electrolyte, potassium, should also be immediately withdrawn from tissue cells would not, on teleological grounds, be expected.

They found the potassium to have a concentration in the urine three times as great as that in cell water, indicating that cell water is retained in the plasma, whereas cell electrolytes, unsuitable for plasma construction, are excreted.

Ingestion or infusion of a variety of salts — sodium sulfate, ammonium chloride, urea and so forth — causes an extra excretion of potassium in the rabbit,³⁹ dog⁴⁰ and man.⁴¹ Wiley and Wiley⁴² followed the process somewhat more closely in a man.⁴² They found that a normal man can be dehydrated to an extent of about 1.5 per cent of his body weight without any great disturbance of salt balance, presumably because of the ability of the organism to concentrate its fluids to some extent. With more marked dehydration — to 5 per cent of body weight — there was an initial loss of sodium and chloride and a persisting loss of potassium, which indicated that, although extracellular fluid is probably the first to respond to water deprivation, there is also a loss of cellular water. When further loss of water was avoided, there was a continued loss of body potassium and a retention of sodium, denoting that a shift from cells to blood serum and interstitial fluids was taking place. When, finally, water was administered in amounts sufficient to restore the original water content of the body, sodium was lost and potassium was retained. The authors concluded that most of this water was thus retained

restricted their diet owing to the symptoms of their disease, and Riggs, Reinhold, Boles and Shore⁸ have recorded a somewhat lower average serum protein concentration in a group of ulcer patients (6.7 gm. per 100 cc.) than in a control group (7.2 gm. per 100 cc.). Since, as Taylor and others⁴ point out, the serum protein level is maintained at the expense of body protein and a deficit of 1 gm. of serum protein indicates on the average a depletion of 30 gm. of tissue protein,⁹ a moderate depletion of serum protein may indicate a substantial loss of protein from the body. In addition, surgeons have almost universally reduced the intake of patients undergoing surgery of the gastrointestinal tract. Intakes of 80 to 2200 calories a day are probably typical of this kind of treatment.⁹ Far from helping either the patient or the surgeon, this procedure, or the depletion of protein resulting from it, causes edema of the gastrointestinal tract, which impedes the surgeon, slows emptying time and promotes vomiting, thus delaying recovery.¹⁰⁻¹⁴ Since the total store of protein in an average adult body is around 2 kg., representing in the hydrated state as much as 11 kg., which if no other source of food were available would supply the basal caloric requirements of the body for only five days or thereabouts, it can be understood that starvation of a patient for five days to a week after operation may seriously deplete the available stores of body protein. A good part of these stores consists of muscle protein, which can hardly be considered as an inert material like fat. This depletion undoubtedly contributes largely to the asthenia seen in patients who have undergone major surgical intervention.

The second factor contributing to the deficit of protein in injury and illness appears to be a regular response to acute illness, whether it be the result of infection, trauma or burn. This toxic loss of nitrogen reaches a maximum on the fourth to the eighth day after the trauma,^{15, 16} and may entail in a ten-day period the loss of as much as 137 gm. of nitrogen, over 850 gm. of dry protein or as much as 4 kg. of body substance. There is a concomitant rise in temperature and a parallel increase in basal oxygen consumption. In trauma, burns and hemorrhagic shock, there is an increase in blood sugar,¹⁷ which according to some¹⁸ may be an unrelated phenomenon, but in the view of others¹⁹ it is certainly a part of the same mechanism. According to the latter, it represents the breakdown of tissue protein, either to supply glucose to meet the needs of the body for extra sugar in an emergency or to supply building blocks for repair in the damaged areas. However beneficial the immediate effects of an increase in blood sugar may be, its continuance can hardly fail to be harmful to the body. Whatever its function, its immediate stimulus may be the secretion of the gluconeogenic hormone of the adrenal cortex.¹⁹

the gaining of other information that may aid importance in promoting normal educational development. But before any of these are undertaken, of a important thing is to find out whether ever a child has normal vision. With this work enhanced shall be better qualified to evaluate prohibits wounding fixtures, optical aids and of to toxic damagnal devices so highly publicized. globin, prevents may be reached that is worthy o intestinal activity medical and educational traditic muscular strength. to Lieutenant Commander E. I situation an adequate for calling the most recent typ must be made available nation.

In many circumstances, even not be maintained by mo be had to parenteral admin

REFERENCES
may be employed, since it is determining acuity of vision
experimentation that an anithia: J. B. Lippincott Co
nitrogen balance by the intrawing. Test objects for il
dog plasma as the only source of ard for testing vision
however, metabolized in a sections of the Section on
manner when injected than it is ation, Atlantic City
mouth,^{22, 23} and there is some doubled. 213:519, 1935.
plete protein.²⁴ The quantities thych. Ophth. 24:924.
jected are too large to permit its us
protein food.

Attention has recently been directed mixtures of amino acids produced by t hydrolysis of casein as a ready source of building blocks. Shohl, Butler, Blackfa Lachlan²⁵ were able to keep infants in p Due sufficient nitrogen balance when such cas" by administered orally or parenterally, we 1944, source of protein. Elman^{24, 26} has given a The 300 gm. daily for three days in a 5 per cent of He claims as advantages of the method thord the gastrointestinal tract without starving the tient, extends the limits within which sur be employed by improving the preoperati facilitates the surgical intervention itself by ing edema in the gastrointestinal tract an mizes postoperative complications. Others¹⁶ with these conclusions.

Others workers,^{4, 10, 15} without renouncing of the intravenous route where it is necessary had recourse to the oral administration of protein diets, reinforced by fat and hydrate. If the patient is unable to take naturally by mouth, they can be administer intubation. When feasible, this method permi administration of far more concentrated solu. or even mixtures, than can be given by vein. V it is considered that Cuthbertson¹⁵ found that containing as high as 230 gm. of protein and calories failed to eliminate the period of nega nitrogen balance, the obvious difficulties of giv protein by vein in a 3 to 5 per cent solution can realized.^{10, 23} This should not, however, become matter for controversy the simplest method shou

ve outlines resembling the coast of Maine. Note the occurrence of the lesion at the lower end of the femur. In the lateral view you can see how the lesion is extending into the bone from without. There is another case showing exactly the same thing.

So far as I am concerned, this man had a neurofibroma. I shall, however, cover myself a little bit.

CLINICAL DIAGNOSIS

Benign giant-cell tumor of femur.

DR. ALBRIGHT'S DIAGNOSIS

Neurofibroma of femur.

ANATOMICAL DIAGNOSIS

Neurofibroma of femur.



FIGURE 1. *Anteroposterior and Lateral Roentgenograms of the Femur.*

The question arises, Why was there a periosteal change in the x-ray films? I think that he had a fracture and that the periosteal proliferation was due to that. I have seen this same kind of periosteal reaction in an eosinophilic granuloma, but that is a poor second choice. And any other diagnosis I can think of is equally poor.

A PHYSICIAN: What about malignant disease?

DR. ALBRIGHT: Do neurofibromas ever become malignant?

DR. JOSEPH AUB: Yes.

DR. CHARLES S. KUBIK: Have we ever had a case with sarcomatous degeneration?

DR. BENJAMIN CASTLEMAN: Yes.

DR. KUBIK: Von Recklinghausen's disease, with other tumors?

DR. CASTLEMAN: Yes; I remember at least one, and I believe we have had others.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Because of the cystic character of the lesion, this patient was operated on with a preoperative diagnosis of benign giant-cell tumor. At operation the surgeon made a window in the very thin cortex, the surface of which was extremely rough, and a large amount of yellowish, friable and, in places, semi-liquid material poured out. The surgeon removed all this material with a curet, leaving a thin shell of bone around a cavity that included both condyles and extended up the femur for about 6 cm. I saw the material at the time of operation and thought that it looked grossly like a benign giant-cell tumor. I did a frozen section and could not see any giant cells, but I did see some foam cells, which are often present in a giant-cell tumor. When the final sections came through, it proved to

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

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CASE 30401

PRESENTATION OF CASE

A forty-five-year-old man, a funeral director, entered the hospital complaining of pain and swelling of the left knee.

Two years before admission the patient first noted minor pains in the left knee, which he attributed to arthritis. For six months prior to entry he noticed, while walking, that the left knee felt insecure. Five weeks prior to entry, while walking on the street, the knee suddenly gave way from under him. There was no pain, but swelling occurred for the first time. He consulted a physician, who made x-ray studies of the knee and told him that he had a "bone tumor." The leg was placed in a posterior mold from heel to groin. He remained entirely comfortable until admission to this hospital. There had been no chills or fever or any redness about the knee. He had had no pain in any other joint.

So far back as he could remember he had had multiple small nodules on the extensor surfaces of the arms and the anterolateral surfaces of the thigh and legs. These had not increased in size or number and had never been painful.

Physical examination showed a well-developed and well-nourished man in no acute discomfort. There were multiple firm, ovoid, freely movable, nontender, subcutaneous nodules on the dorsal surfaces of both forearms and of the left thigh. There was a tender swelling over the lower portion of the left femur. Most of the tenderness was over the medial parapatellar aspect of the condyle of the femur. Examination of the heart, lungs and abdomen was negative.

The blood pressure was 130 systolic, 82 diastolic. The temperature, pulse and respirations were normal.

The urine was normal. The blood showed a white-cell count of 10,300, with 76 per cent neutrophils, and a hemoglobin of 15.8 gm. per 100 cc.

A roentgenogram of the lower end of the left femur showed destruction of the normal bony structure with preservation of most of the cortex. The cortex was thin, and anteriorly and laterally appeared to be broken through, with an accompanying

periosteal reaction (Fig. 1). The joint surfaces were intact. There was no soft-tissue mass visible around the bones. Films of the spine showed that the left intervertebral foramen between the second and third cervical vertebrae was increased in size, and there were pressure defects involving the bodies of the second and third vertebrae in this area. Stereoscopic views showed flattening of the pedicles of the third cervical vertebra and probable, but not definite, slight enlargement of the intervertebral foramen. Films of the skull, arms and forearms were normal. A chest roentgenogram showed scarring in both apices, with calcification and fibrosis. There was scalloping of the inferior margins of several of the ribs, particularly the seventh on the left, but no definite soft-tissue masses were seen.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. FULLER ALBRIGHT: The diagnosis depends on the x-ray films and is not too difficult, I believe. Let us look at the films.

DR. MILFORD SCHULZ: This is the film of the knee made some time before entry. Here are the films taken at the time of his visit to the hospital. Between these examinations he developed a little more periosteal reaction.

DR. ALBRIGHT: I may be "all wet," but if this is not neurofibromatosis I shall be greatly surprised. The patient had multiple subcutaneous nodules. He had evidence of multiple enlargement of the nerves, with definite enlargement of one cervical foramen. He had a lesion in a very characteristic location for a neurofibroma, namely, the lower end of the femur.

The bone lesion in neurofibromatosis is not strictly a bone lesion but is an encroachment of a tumor of the nerve on the bone. The lesion is apt to occur where nerves enter the bone. In the anteroposterior view it often looks like a cyst; and in the lateral view one can often see — but not in this case — that the cyst-like appearance is due to a lesion on the outside extending into the bone. The most frequent site of the bone lesions in neurofibromatosis is the lower end of the femur. I am so confident that this is a case of neurofibromatosis that I brought along a few slides of some other cases for comparison. I will not consider any other diagnosis.

Here is a case of neurofibromatosis showing brown spots on the skin and subcutaneous nodules. The brown spots are characteristic. They have smooth edges like the coast of California, which are distinctly different from those in the disease that I have recently been interested in, osteitis fibrosa disseminata or what is perhaps a better name "polyostotic fibrous dysplasia," where the brown skin lesions

*On leave of absence.

matous. We reviewed the slides of the original tumor, of which we had made a large number,

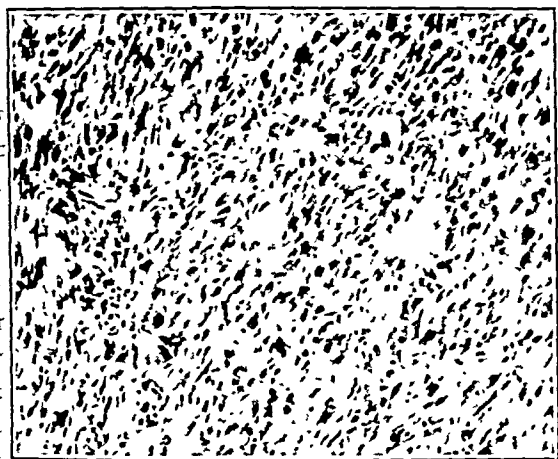


FIGURE 4. Photomicrograph of the Recurrent Tumor.

but could find not the slightest evidence of malignancy.

CASE 30402

PRESENTATION OF CASE

A six-week-old girl was admitted to the hospital because of "blue spells."

The infant was one of twins, delivered after an easy, normal labor, and weighed slightly over 4 pounds at birth. At the age of two weeks it was noted that she had difficulty getting her breath while feeding. This symptom persisted. Two days before entry she was taken to a pediatrician, who found an enlarged heart and liver. On the day of admission she had three episodes of cyanosis, the first being the severest and lasting forty minutes.

Physical examination showed a well-developed, fairly well-nourished, slightly dusky infant. The lungs were clear. The heart was markedly enlarged to the left, extending 2 cm. outside the midclavicular line and 3 cm. to the right of the sternum. No murmurs were heard. The sounds were distant. The liver was palpable 3 cm. below the right costal margin.

The temperature was 98°F., the pulse 120, and the respirations 60 to 80.

Examination of the blood showed a white-cell count of 10,640, with 46 per cent neutrophils, 8 per cent large and 44 per cent small lymphocytes and 20 per cent eosinophils.

X-ray examination of the chest showed a definitely enlarged heart without a characteristic configuration. An electrocardiogram revealed a sinus tachycardia, with a rate of 200, slight left-axis deviation, deep S₁, S₂ and S₃ and late inversion of T₁ and T₂; T₃ was upright. A repeat electro-

cardiogram seven days later showed no appreciable change.

The child was placed in an oxygen tent. The respirations fell to about 55 and she had no "cyanotic spells," but whenever she was out of the tent for half an hour to an hour the color became poor. Otherwise her condition remained unchanged until the eighth hospital day, when she started to cough and became cyanotic while being fed. She was put back into the oxygen tent but died five minutes later.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS: The electrocardiogram is obviously abnormal. It is more usual at this age to see right-axis deviation than left, although the latter may be present. Of course the T wave inversion in Leads 1 and 2 is abnormal. Other than that there is nothing about the pattern that gives any specific help. A heart rate of 200 does not suggest paroxysmal tachycardia in an infant. Sinus tachycardia as a direct result of heart disease is likelier.

In discussing the differential diagnosis there are three groups of congenital conditions — and I think it is obvious that this child had a congenital condition — that should be considered. The first group includes the mechanical defects of the great vessels, such as transposition of the trunks, defects of the valves, for example, aortic stenosis and pulmonary stenosis, and septal defects — auricular and ventricular. In order to make such a diagnosis one must have more evidence than I have here. No characteristic murmurs were heard. In a great many congenital defects an electrocardiogram is helpful in that high voltage and right-axis deviation are present, this being particularly true in infants who are deeply cyanotic. In this case, however, the electrocardiogram gives no assistance. One thing that helps a little in narrowing the field down is the degree of cyanosis. The fact that it was moderate and not constant rules out the congenital malformations characterized by marked cyanosis, transposition of the great trunks with septal defect, cor biloculare with persistent truncus and so forth. Those conditions are usually compatible with life for only a few days or weeks.

Another condition that must be considered is the tetralogy of Fallot, which usually is accompanied by more cyanosis than was noted here. Cyanosis, however, is not always present before the age of two. I believe that that diagnosis can be ruled out by the absence of characteristic murmurs and of evidence of right-axis deviation in the electrocardiogram. More frequent defects, such as an auricular septal defect, ventricular septal defect and patent ductus arteriosus, do not usually produce death at this age unless they are extremely large, and two of these conditions are associated with

be a neurofibroma with areas of degeneration that contained a large number of foam cells (Fig 2).

DR. LAURENCE L. ROBBINS: The lesions of neurofibroma of bone that we see usually have a charac-

bone, although it may have started in a periosteal nerve and, instead of extending outward, extended inward.

ADDENDUM

DR. CASTLEMAN: The patient was well and free from symptoms for the following ten months, when he noticed enlargement of the knee. A roentgenogram (Fig. 3) showed an area of destruction just above the condyle that was not present in previous films. It also showed considerable periosteal proliferation extending up the shaft, with similar changes about the cavity filled with bone chips. A chest plate was normal. Since it was thought that the tumor had recurred and had become malignant, a mid-thigh amputation was performed.

The tumor involved the lowermost 10 cm of the femur and had extended into the surrounding tissues, especially the popliteal and suprapatellar regions, to form large soft-tissue tumor masses. There was no involvement of the tibia, although the articular cartilage was eroded. Microscopically the change from the original tumor was striking. The cells were large and atypical, and mitoses were numerous (Fig. 4). This is an example, therefore, of a case of

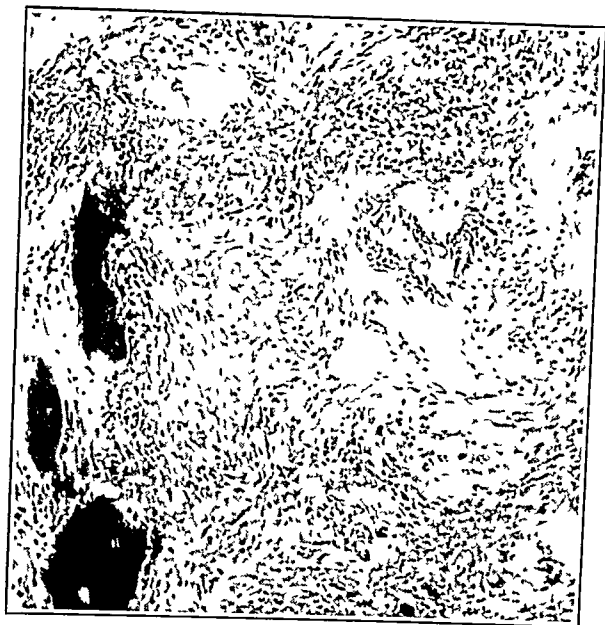


FIGURE 2 Photomicrograph of the Tumor

teristic appearance. They erode the periosteal margins of the bone, producing an indentation of

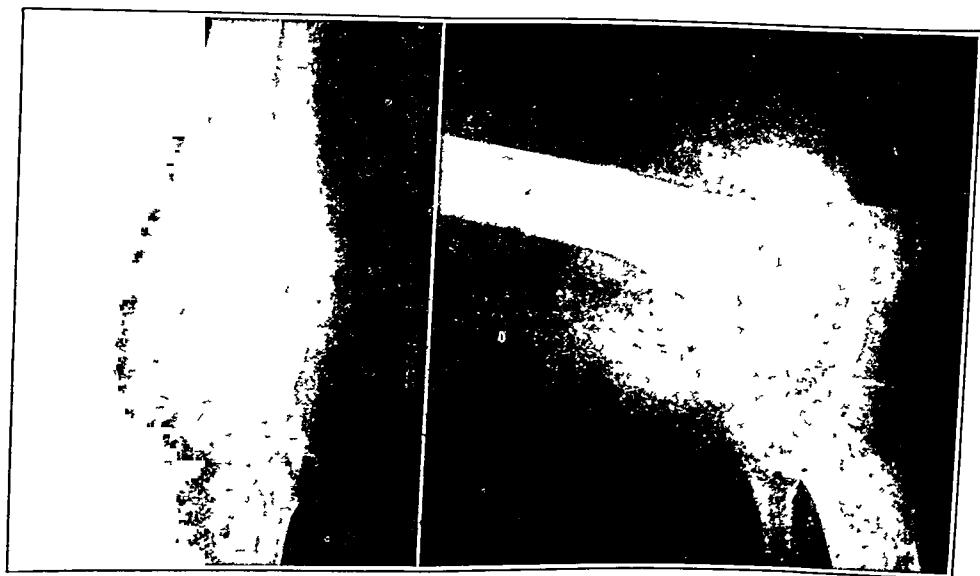


FIGURE 3 Anteroposterior and Lateral Roentgenograms of the Femur
Note the large, soft-tissue masses. The bone lesion is filled with bone chips. There is an area of destruction on the medial margin of the lower shaft and condyle.

the cortex. In this case, from the appearance of the x-ray, the lesion seems to have arisen within the

generalized neurofibromatosis in which one of the benign neurofibromas involving bone became sar-

ght. The valves were normal. There was a slightly patent foramen ovale, which was probably of no significance. The aorta, just beyond the arch and at the level of the ductus arteriosus, which admitted a 2-mm. probe, was slightly narrow, so that I think that we can make a diagnosis of slight coarctation of the aorta. The liver was normal in size for a child of this age, weighing 125 gm., and all the other organs were normal.

Microscopic examination of the heart muscle proved that this was a case of glycogen-storage (von Gierke's) disease. The myocardial fibers were

filled with glycogen, and even after fixation in formalin, in which ordinarily the granules are dissolved out, we were able to find the deposits of glycogen. There were relatively few granules in the liver. This falls in with the type of disease that is confined almost wholly to the heart, without involvement of the liver or kidneys.

DR. WILLIAMS: Was a urine examination reported? It is not given in the abstract, and it might have been helpful in the diagnosis if it had shown persistent acetonuria.

DR. CASTLEMAN: No examination is recorded.

characteristic murmurs, which this patient did not have.

One anomaly falling into this group that is consistent with the findings is abnormal origin of a coronary artery. Cases have been reported in which one of the coronary arteries, usually the left, rises from the pulmonary artery. In other cases there is only one coronary artery, which arises from the aorta. Ten years ago Dr. Paul D. White reported a case of an anomalous coronary in a boy three and a half months old who died following a series of attacks of cyanosis, sweating and dyspnea.* The child's electrocardiogram was grossly abnormal, with the most important changes in Leads 1 and 2, as they were here. The findings of cardiac enlargement without murmurs and a rather characteristic electrocardiogram are entirely in keeping with that diagnosis.

The second group of congenital disorders is that characterized by changes in the heart muscle itself. The most frequent is congenital idiopathic hypertrophy. Obviously the name is unsatisfactory. The group so designated is getting smaller all the time as more specific causes for hypertrophy are found. Many cases remain, however, in which the only finding at death is that of a large heart uncomplicated by any other anatomical finding. The findings in this case — the early death, the paroxysms of cyanosis and so forth — are entirely in keeping with this diagnosis. In the same group one must also consider von Gierke's or glycogen-storage disease, in which there is a disorder of glycogen metabolism. The most characteristic finding is that of hepatic enlargement. The heart may or may not be enlarged, but in some cases the heart enlarges proportionately more than the liver. Usually this is a chronic disease and patients live for years, but early deaths have been reported. I was interested in the description of the liver, which was said to have been definitely enlarged. That may mean something. The spleen was not enlarged. The absence of splenomegaly is another characteristic of glycogen-storage disease.

The third group to be considered is that characterized by lesions in the circulatory system outside the heart, especially in the lungs. A number of cases have been reported in these conferences — one of which I misdiagnosed — in which the chief lesion was a developmental defect of the pulmonary circulation. It usually consists of a lack of differentiation of the small radicles and capillaries into their usual subgroups which results, ordinarily, in a primitive, narrow circulation that obstructs the pulmonary flow. Such cases have been reported with findings similar to these. The only thing lacking in this case is an electrocardiographic pattern showing evidence of right-axis deviation.

*Bland, E. F., White, P. D., and Garland, J. Congenital anomalies of coronary arteries: report of unusual case associated with cardiac hypertrophy. *Am. Heart J.* 8:787-801, 1933.

In reaching a final diagnosis, there is one differential point of the greatest importance that cannot be answered with certainty. Was the enlarged liver the result of heart failure or of intrinsic liver disease (glycogen-storage disease)? A definite statement about the neck vessels might have answered that question, because when the liver enlarges as a result of heart failure, the neck veins almost invariably either are distended or show characteristic pulsation. Not having that statement I am forced to make a differential diagnosis that includes the three conditions, and I shall name them in the order of probability: idiopathic cardiac hypertrophy, glycogen-storage disease and an anomalous coronary artery. I cannot make a diagnosis of septal defect, valvular defect or an anomaly of the great vessels.

DR. T. DUCKETT JONES: I should like to ask Dr. Williams whether he thinks that, in general, the findings in the neck veins are as significant in children as they are in adults.

DR. WILLIAMS: Venous pulsation probably is. One does not often observe distended neck veins except in cases with a high degree of obstruction to the venous circuit. I do not see a great many infants, but my impression is that the neck veins show abnormal pulsations in the presence of increased venous pressure, even in infants.

DR. JONES: I have been impressed with the facts that in right-sided failure in young children the liver is easily palpable, and that neck signs, which might lead to an early diagnosis, are usually absent.

CLINICAL DIAGNOSIS

Congenital heart disease (idiopathic hypertrophy).

DR. WILLIAMS'S DIAGNOSIS

Congenital idiopathic cardiac hypertrophy?
Glycogen-storage (von Gierke's) disease?
Anomalous coronary artery?

ANATOMICAL DIAGNOSES

Glycogen-storage (von Gierke's) disease of heart.
Cardiac hypertrophy.
Coarctation of aorta, slight.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr. White saw this patient in consultation; he thought that the changes were consistent with a congenital anomaly of the coronary arteries and referred to the patient whom he had seen before.

The autopsy showed an enlarged heart, weighing 50 gm., which is about two and a half times the normal weight for a child of this age. The enlargement was uniform throughout the chambers, but slightly more prominent on the left than on the

On the basis of these studies and the reports of a number of clinicians, the Russian workers urged the use of this antireticular cytotoxic serum for the treatment of a wide variety of conditions, which include all types of infectious disease, particular attention being made of typhus fever, puerperal and necrologic sepsis, rheumatic fever, tonsillitis, unresolved pneumonia, lung abscess and infectious diseases of the nervous system. They also believed that their clinical observations had established the therapeutic efficacy of this serum in war injuries of various sorts, including fractures, frostbites, second-degree and third-degree burns, early and late purulent infections of the cavities and tissues, and infected lesions of the eye. It was particularly effective in slowly healing infected wounds. They even felt justified in recommending its use in the treatment of neuritis, meningoencephalitis, disseminated sclerosis, senile and presenile psychoses, and schizophrenia. Some "encouraging results" were also obtained in the treatment of peptic ulcer, eczema and other "trophic" disturbances. Although not included in the list of indications, it is apparent that at least the senior author also thought that this substance might give favorable results in the prevention and treatment of cancer and senility. In fact, it was this author's interest in the latter that was largely responsible for the studies that led to the development of the serum.

These results may seem rather fantastic to "hard-boiled" American scientists who are accustomed to have extensive and thoroughly documented evidence presented for any new discovery of such far-reaching significance before they consider it even plausible. Before taking it seriously, they would undoubtedly like to see this work repeated by many independent workers under carefully controlled conditions. Unfortunately, the details of the Russian observations are not readily accessible in a form in which they can be properly evaluated by workers in this country. Until they are, one must consider these findings with an open mind.

At the time of the publication of these reports, the editor of the *American Review of Soviet Medicine* was apparently quite enthusiastic about the possibilities offered by this serum. Indeed, he was moved to write a note in preface to the issue, which

ended in an appeal to expedite further studies with this serum. Clinical investigators in this country, who are not always easy to convince and who are usually quite wary of accepting such cure-alls, will undoubtedly prefer to await more detailed evidence of the efficacy of this agent before embarking on any clinical trials of their own. If one may judge from the tone of an editorial note printed in the following issue of the *American Review of Soviet Medicine*, it is evident that the former note was not enthusiastically received.

MASSACHUSETTS MEDICAL SOCIETY

EXECUTIVE COMMITTEE OF THE COUNCIL

On August 30, 1944, the Executive Committee of the Council, on the recommendation of the Committee on Membership and representatives from the supervising censors, took the following actions:

Allowed the following named fellows, applying for retirement and with all dues paid and in good standing, to retire under the provisions of Chapter I, Section 5, of the by-laws, such retirement to be effective as of January 1, 1944:

Cavanaugh, Thomas E. (Hampden), 293 Bridge Street, Springfield.
Dexter, Fred F. (Hampden), 151 Maple Street, Springfield.
Gorham, George H. (Norfolk), 91 Crest Avenue, Chelsea.
Johnson, Erik St. J. (Middlesex South), 8 Follen Street, Cambridge.
Ruble, Wells A. (Nonresident), 1929 East Glenoaks Boulevard, Glendale, California.

Allowed the following named fellows, applying for retirement, to retire with remission of dues owed the Society under the provisions of Chapter I, Section 5, of the by-laws, such retirement to be effective as of January 1, 1944:

Avedisyan, A. D. (Middlesex South), 164 Huntington Avenue, Boston.
Barton, John A. (Worcester North), 61 Fox Street, Fitchburg.
Ford, J. Francis (Norfolk), 8 Walter Street, Roslindale.
Hunt, Daniel L. (Suffolk), Hotel Vendome, Boston.
Nightingale, James (Worcester), 14 Puritan Avenue, Worcester.
Sargent, Oscar F. L. (Nonresident), 45 North Main Street, Farmington, New Hampshire.
Stevens, Harry L. (Bristol South), 133 Kempton Street, New Bedford.

Reinstated the following named physician, under the provisions of Chapter I, Section 10, of the by-laws, who had been deprived of fellowship for the nonpayment of dues, provided his arrears in dues at the time he was dropped plus the dues for 1944 be paid to the treasurer of the Society:

Wainshel, P. W. (Essex South), 92 South Common Street, Lynn.

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THE BLUE TRIANGLE

It will be readily appreciated that there will always be a large number of people who, for one reason or another, have not covered their catastrophic medical costs by prepayment insurance placed with commercial companies or with the Blue Shield or the Blue Cross, or both.

For about two years committees of the Massachusetts Medical Society and of the Massachusetts Bankers Association have been jointly considering a dignified postpayment plan for medical costs. The Association has gone into this plan extremely thoroughly, consulting proper authorities regarding the strategies, the legal aspects and the technical machinery of putting such a plan into effect.

The Massachusetts Medical Society authorized its committee to participate in the planning and to initiate the program after the plans had been completed.

The groundwork has been accomplished. The plan — the Blue Triangle — is ready and will soon be put into operation. All members of the Massachusetts Medical Society will receive detailed information through their local banks. Each member should become thoroughly familiar with the opportunities provided by the plan and should make them known to those of his patients who might benefit thereby.

ANTIRETICULAR CYTOTOXIC SERUM

CONSIDERABLE though brief interest was manifested in this country recently in a serum developed in Soviet Russia that was reported to have remarkable curative and healing properties. Some of the details concerning this remarkable discovery were presented at a special conference of clinicians and biologists that took place in Ufa in July, 1942. A brief report of the experimental and theoretical background and of some of the clinical applications of this serum is given in a series of papers published in the December, 1943, issue of the *American Review of Soviet Medicine*.

Over a number of years a group of Russian investigators, under the leadership of Professor A. A. Bogomolets, have conducted an extensive series of investigations on the effects of cytotoxic serums. Their results have led them to believe that small doses of antireticular cytotoxic serum stimulate mesenchymal cells, whereas larger doses block these cells. To prepare organotoxic immunizing serums for any animal, they use desiccated cells from another type of animal. Using cells of the spleen and marrow, they obtain serum that is cytotoxic to mesenchymal cells and that Doctor Bogomolets calls "antireticular." For use in human beings, the antireticular cytotoxic serum is prepared by immunizing animals with an antigen derived from the spleen and marrow of human cadavers. These organs must be obtained not later than six to ten hours after death in cases in which there has been no evidence of infectious disease.

- CHERRY, HARRIET E., 156 Maple Street, Springfield.
Tufts College Medical School, 1942.
- CLEVELAND, HAROLD F., 462 Belmont Avenue, Springfield.
Middlesex University School of Medicine, 1920. Sponsor:
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ovitz, 4 Chestnut Street, Springfield.
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Mid-West Medical College, 1935. Sponsor: Arthur H.
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College of Medical Evangelists, 1942.
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Brendan D. Leahey, *Secretary*
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Sponsor: Clifford A. Butterfield, 13 Bradlee Road,
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North Carolina.
Middlesex University School of Medicine, 1937. Sponsor:
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- CALIVA, FRANCIS S., 122 Highland Avenue, Malden.
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- SYLVESTER, ROWLAND E., 11 Fern Street, Auburndale.
Boston University School of Medicine, 1943.

Alexander A. Levi, *Secretary*
481 Beacon Street, Boston

NORFOLK DISTRICT

- ANDERSON, RUTH M., 61 Hastings Street, West Roxbury.
Boston University School of Medicine, 1940.
- BANDEIAN, ALICE M. K., 199 Canton Street, Westwood.
Boston University School of Medicine, 1941.
- BERENBERG, WILLIAM, 810 West Roxbury Parkway, Brook-
line.
Boston University School of Medicine, 1940.
- BROWN, FRANCIS H., 31 Monadnock Road, Wellesley Hills.
Tufts College Medical School, 1941.
- CHIAMPA, FRANCIS P., 122 Riverway, Boston.
Tufts College Medical School, 1939.
- FAVOUR, CUTTING B., 306 Riverway, Boston.
Johns Hopkins University School of Medicine, 1940.
- GATEMAN, MURRAY, 120 Hutchings Street, Boston.
Middlesex University School of Medicine, 1934. Sponsor:
Roger T. Doyle, Jamaica Plain. Office, 1550 Tremont
Street, Boston.
- GORE, MAX, 107 Blue Hill Avenue, Roxbury.
Mid-West Medical College, 1937. Sponsor: Max Davis,
Brookline. Office, 311 Commonwealth Avenue, Boston.
- HIGGINS, CLARENCE B., 110 Blue Hills Parkway, Milton.
Middlesex University School of Medicine, 1918. Sponsor:
Carlton E. Allard, 428 Columbia Road, Dorchester.
- HOFFMAN, HOWARD A., 1454 Beacon Street, Brookline.
New York Medical College, 1940.
- JAMES, HARRIET D., 123 Longwood Avenue, Brookline.
University of Minnesota Medical School, 1935.
- JONES, STEWART H., 119 Fuller Street, Brookline.
McGill University Faculty of Medicine, 1933.
- KURZMANN, RUDOLF, State Prison Colony Hospital, Norfolk.
University of Vienna Medical School, 1921. Sponsor:
Louis A. Sieracki, 71 Winter Street, Norwood.
- LEVIN, SIDNEY, 74 Salisbury Road, Brookline.
Tufts College Medical School, 1939.
- Lipsher, Leo, 281 Humboldt Avenue, Roxbury.
Tufts College Medical School, 1924.
- McMACKIN, FRANCIS L., 206 Riverway, Boston.
Boston University School of Medicine, 1941.
- MESHOKER, EDWARD, 14 Sonoma Street, Roxbury.
Kansas City University of Physicians and Surgeons, 1938.
Sponsor: Bernard Weiss, 736 Morton Street, Mattapan.
- MOORE, THOMAS J., 147 Ashmont Street, Dorchester.
Middlesex University School of Medicine, 1933. Sponsor:
Cyril M. Lydon, 276 Bowdoin Street, Dorchester.
- MOSTOFI, FATHOLLAH K., 97 Binney Street, Boston.
Harvard Medical School, 1939.
- PROUT, CURTIS, 215 Heath Street, Chestnut Hill.
Harvard Medical School, 1941.
- RUBEN, MAURICE R., 40 Hansborough Street, Dorchester.
Boston University School of Medicine, 1939.
- SHAPIRO, ELI, 484 Blue Hill Avenue, Roxbury.
Middlesex University School of Medicine, 1937. Sponsor:
George Robbins, Brookline. Office, 416 Marlboro Street,
Boston.
- STERMAN, IDA A., 132 Clark Road, Brookline.
Boston University School of Medicine, 1940.

Remitted the dues owed the Society, plus those of the present year 1944, of the following named fellow, who is ill and incapacitated, under the provisions of Chapter I, Section 6, of the by-laws:

Bartlett, Bernice A. (Essex North), 11 Haseltine Street, Bradford.

Accepted the resignations of the following named fellows, all with dues paid and in good standing, under the provisions of the by-laws, Chapter I, Section 7, the date of resignation to be as of January 1, 1944:

Friedgood, Harry B. (Norfolk), The Shelton Clinic, 921 Westwood Boulevard, Los Angeles 24, California.
Harris, Ella F. (Worcester), 845 West State Street, Trenton 8, New Jersey.
Plouffe, Bernard L. (Worcester), 11 Hill Street, Webster.
Smith, John Hall (Middlesex South), Middlesex University, Waltham.

Accepted the resignation and remitted the dues owed the Society of the following named fellow under the provisions of the by-laws, Chapter I, Section 6 and Section 7, the date of resignation to be as of January 1, 1944:

Haskell, Helen S. (Hampshire), 135 East 65th Street, New York 21, New York.

Deprived the following named fellows of the privileges of fellowship because of arrears of dues owed the Society under the provisions of the by-laws, Chapter I, Section 8:

Cargen, Samuel S. (Suffolk), 49 North Russell Street, Boston.
Coyne, John A. (Norfolk), 1162 Beacon Street, Brookline.
Dunscombe, William C. (Nonresident), South Puerto Rico Sugar Company, Ensenada, Puerto Rico.
Ein, Johannes E. (Nonresident), Bellevue Hospital, 111 East 65th Street, New York City.
Everett, Winchester W. (Middlesex South), 270 Commonwealth Avenue, Boston.
Fennelly, Daniel J. (Bristol South), 276 Winter Street, Fall River.
Ferrucci, Joseph (Middlesex South), 270 Concord Street, Framingham.
Hagerty, Harry J. (Worcester), 14 Ekman Street, Worcester.
Johnson, Alfred E. (Franklin), 58 Federal Street, Greenfield.
Kelley, Edward J. (Middlesex South), 380 Mt. Auburn Street, Watertown.
McEwen, Herbert B. (Norfolk), 118 Queens Avenue, New Westminster, B. C., Canada.
Miller, Robert T., Jr. (Plymouth), Mountain Lake, Lake Wales, Florida.

The personnel of the Committee on Membership is as follows: Harlan F. Newton, *chairman*; John E. Fish; Peirce H. Leavitt; Sumner H. Remick; and Samuel N. Vose. The representatives of the supervising censors are as follows: William H. Allen, H. Quimby Gallupe and Albert E. Parkhurst.

MICHAEL A. TIGHE, M.D., *Secretary*
Executive Committee

APPLICANTS FOR FELLOWSHIP

PUBLISHED IN ACCORDANCE WITH THE PROVISIONS OF THE BY-LAWS (CHAPTER V, SECTION 2) as amended May 1, 1942

BARNSTABLE DISTRICT

SMYTH, HENRY F., Box 232, Pocasset.
University of Pennsylvania School of Medicine, 1897.
Julius G. Kelley, *Secretary*
Barnstable County Sanatorium, Pocasset.

BERKSHIRE DISTRICT

BOWMAN, ROSE M., 103 Notch Road, North Adams.
Middlesex University School of Medicine, 1931. Sponsor: James W. Bunce, 85 Main Street, North Adams.
BOWMAN, WILLIAM E., 57 Main Street, North Adams.
Middlesex University School of Medicine, 1931. Sponsor: James W. Bunce, 85 Main Street, North Adams.
CAMPBELL, DONALD E., Stockbridge.
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DONEY, FRANK C., 271 Tyler Street, Pittsfield.
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JOSLIN, ERIC F., West Stockbridge.
Albany Medical College, 1933.
MARCOTTE, REO J., 741 North Street, Pittsfield.
University of Michigan Medical School, 1936.
N. Newall Copeland, *Secretary*
131 North Street, Pittsfield.

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GRANT, MAURICE D., 174 North Washington Street, North Attleboro.
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William J. Morse, *Secretary*
34 Sanford Street, Attleboro.

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GESING, EMIL J., 197 Prospect Street, Lawrence.
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Harold R. Kurth, *Secretary*
57 Jackson Street, Lawrence.

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FILIP, B. JOHN, 416 Essex Street, Salem.
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HARRIGAN, FRANCIS J., 56 Washington Square, Salem.
Middlesex University School of Medicine, 1936. Sponsor: Philip J. Finnegan, 82 Washington Square, Salem.
MUSMAN, SAMUEL, 484 Western Avenue, Lynn.
Middlesex University School of Medicine, 1933. Sponsor: Jacob B. Bakst, 174 South Common Street, Lynn.
PARKER, HARRY W., 17 Broad Street, Lynn.
University of Lausanne, 1938. Sponsor: Bernard Apple, 281 Ocean Street, Lynn.
POTASH, JACOB, 155 Broadway, Lynnfield.
Middlesex University School of Medicine, 1933. Sponsor: Ellis Michelson, 81 North Common Street, Lynn.
ROSS, LAWRENCE, 19 Chester Square, Annisquam.
Harvard Medical School, 1941.
SHUB, WILLIAM E., 602 Boston Street, Lynn.
Middlesex University School of Medicine, 1938. Sponsor: Philip J. Finnegan, 82 Washington Square, Salem.
Henry D. Stebbens, *Secretary*
26 Chestnut Street, Salem.

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BLAKER, SAMUEL I., 262 Riverdale Street, West Springfield.
Middlesex University School of Medicine, 1926. Sponsor: George L. Steele, 20 Maple Street, Springfield.

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Boston University School of Medicine, 1939.
- SHAPIRO, ELL, 484 Blue Hill Avenue, Roxbury.
Middlesex University School of Medicine, 1957. Sponsor:
George Robbins, Brookline. Office, 416 Marlboro Street,
Boston.
- STERMAN, IDA A., 152 Clark Road, Brookline.
Boston University School of Medicine, 1940.

VANDAM, LEROY D., 235 Park Drive, Boston.
New York University College of Medicine, 1938.

Charles J. E. Kickham, *Secretary*
12 Bay State Road, Boston

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- DAIUTE, ELEANOR D., 76 Central Avenue, South Braintree.
Middlesex University School of Medicine, 1936. Sponsor:
Arsham Alemian, 691 Broad Street, East Weymouth.
DORNE, RAYMOND M., 618 Washington Street, Quincy.
Middlesex University School of Medicine, 1936. Sponsor:
Emil Z. Ossen, 1230 Hancock Street, Quincy.
FRANKMAN, WILLIAM, 736 Hancock Street, Wollaston.
St. Louis College of Physicians and Surgeons, 1921. Sponsor:
Frank Belin, 108 Billings Road, Quincy.

Ebenezer K. Jenkins, *Secretary*
Norfolk County Hospital, South Braintree

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- ASIAF, BOLIS G., 107 Prospect Street, Brockton.
Middlesex University School of Medicine, 1936. Sponsor:
George A. Moore, 167 Newbury Street, Brockton.
FARLEY, EDWARD J., 91 Pleasant Street, Stoughton.
Middlesex University School of Medicine, 1937. Sponsor:
Michael F. Barrett, 231 Main Street, Brockton.
SHAPIRO, HARRY, 64 Seaver Street, Stoughton.
Middlesex University School of Medicine, 1931. Sponsor:
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WAITKUS, ALGIRD A., 676 North Main Street, Brockton.
Middlesex University School of Medicine, 1937. Sponsor:
George A. Moore, 167 Newbury Street, Brockton.

Ralph C. McLeod, *Secretary*
Goddard Hospital, Brockton

SUFFOLK DISTRICT

- BRADLEY, STANLEY E., 46 Hereford Street, Boston.
University of Maryland School of Medicine, 1938.
BRASS, BERNARD B., 30 Sea Foam Avenue, Winthrop.
College of Physicians and Surgeons, Boston, 1934. Sponsor:
Jacob J. Abrams, 562 Shirley Street, Winthrop.
BROWN, SYLVAN G., 105 Pleasant Street, Concord, New
Hampshire.
College of Physicians and Surgeons, Boston, 1938. Sponsor:
Seth F. H. Howes, Arizona State Hospital, Phoenix,
Arizona.
DAVIS, PAUL, 541 Commonwealth Avenue, Boston.
Kansas City University of Physicians and Surgeons, 1933.
Sponsor: Carrie I. Felch, 541 Commonwealth Avenue,
Boston.
DUTRA, FRANK R., 25 Shattuck Street, Boston.
Northwestern University Medical School, 1942.
FERREBEE, JOSEPH W., Harvard Medical School, Boston.
Harvard Medical School, 1934.
GREENFIELD, HAROLD B., 14 Coral Avenue, Winthrop.
College of Physicians and Surgeons, Boston, 1937. Sponsor:
Jacob J. Abrams, 562 Shirley Street, Winthrop.
ILLINGWORTH, MYLES H., Boston City Hospital, Boston.
Tufts College Medical School, 1943.
INGALLS, RAYMOND G., 5 Bay State Road, Boston.
Tufts College Medical School, 1920.
LANDRY, CHRISTOPHER L., Boston City Hospital, Boston.
Tufts College Medical School, 1943.
ROIFF, HARRY S., 159 Shurtleff Street, Chelsea.
St. Louis College of Physicians and Surgeons, 1923. Sponsor:
William Paris, 139 Washington Avenue, Chelsea.
ROTHMANN, EVA, 334 Commonwealth Avenue, Boston.
University of Berlin, 1927. Sponsor: Oscar J. Raeder, 270
Commonwealth Avenue, Boston.
TRAUNSTEIN, MAURICE, JR., 41 Bayview Avenue, Winthrop.
University of Vermont College of Medicine, 1942.

Robert L. Goodale, *Secretary*
330 Dartmouth Street, Boston

WORCESTER NORTH DISTRICT

- GROSSMAN, MYER J., 352 Crescent Street, Athol.
Middlesex University School of Medicine, 1933. Sponsor:
Francis X. Dufault, 245 School Street, Athol.
SCHECHTMAN, HAROLD I., 64 Milk Street, Fitchburg.
Middlesex University School of Medicine, 1934. Sponsor:
Joseph D. Quinlan, 44 Prichard Street, Fitchburg.

Edward A. Adams, *Secretary*
44 Oliver Street, Fitchburg

DEATHS

BERMAN — Saul Berman, M.D., of Chestnut Hill
Newton, died September 18. He was in his forty-ninth year.
Dr. Berman received his degree from Harvard Medical
School in 1920. He was formerly resident physician at the
Boston Lying-in Hospital and was the founder of the Fer-
ity Clinic and Laboratory at the Beth Israel Hospital. He
was a member of the Boston Obstetrical Society.
His widow and three sons survive.

GAGNON — Alphonse P. Gagnon, M.D., of Taunton
died August 2. He was in his fifty-third year.

Dr. Gagnon received his degree from Tufts College Medical
School in 1921. He was a member of the American Medical
Association and the New England Society of Obstetrics
and Gynecology.

His widow, a son and a daughter survive.

SPARROW — Charles A. Sparrow, M.D., of Worcester
died September 20. He was in his sixty-first year.

Dr. Sparrow was born in Marion and graduated from
Amherst College in 1906, receiving his degree from Harvard
Medical School in 1909. He was appointed to the staff of
Memorial Hospital in 1916 and in 1925 became head of the
Pediatric Clinic there. He was an associate editor of the
Worcester Medical News, a publication of the Worcester
District Medical Society, as well as a past president of the
society and a councilor of the Massachusetts Medical Society.
He was a member of the American Academy of Pediatrics
and of the New England Pediatric Society.

His widow, a son, a daughter and a sister survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1944

RÉSUMÉ

DISEASES	AUGUST 1944	AUGUST 1943	SEVEN-YEAR MEDIAN
Anterior poliomyelitis..	137	24	15
Chancroid	2	*	*
Chicken pox	192	123	120
Diphtheria	6	5	12
Dog bite	1056	1064	1068
Dysentery, bacillary ..	18	14	15
German measles	57	72	31
Gonorrhea	426	374	432
Granuloma inguinale ..	0	*	*
Lymphogranuloma venereum	49	13	2
Malaria	227	346	281
Measles	34	34	4
Meningitis, meningococcal	27	1	†
Meningitis, Pfeiffer-bacillus	3	1	†
Meningitis, pneumococcal	1	2	†
Meningitis, staphylococcal	0	0	†
Meningitis, streptococcal	0	1	†
Meningitis, other forms	0	0	†
Meningitis, undetermined	2	11	†
Mumps	273	137	143
Pneumonia, lobar	71	76	91
Salmonella infections ..	24	22	13
Scarlet fever	197	248	125
Syphilis	393	418	367
Tuberculosis, pulmonary ..	253	252	269
Tuberculosis, other forms	14	23	25
Typhoid fever	7	3	10
Undulant fever	5	3	4
Whooping cough	261	286	508

*Made reportable in December, 1943.

†Pfeiffer-bac

COMMENT

Interest in the communicable disease situation centers this month on anterior poliomyelitis, both because of the seasonal increase in cases and because of outbreaks in certain other states. At present, the number of cases in Massachusetts is far below that of epidemic years, although greatly in excess of the seven-year median.

Salmonella infections were at nearly double the seven-year median for August. These cases, however, were widely scattered about the state.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Adams, 1; Agawam, 1; Athol, 1; Barre, 1; Belchertown, 1; Boston, 5; Cambridge, 1; Chelsea, 1; Chicopee, 4; Dalton, 5; Deerfield, 4; Fall River, 2; Gloucester, 1; Great Barrington, 1; Groveland, 1; Haverhill, 5; Holyoke, 5; Lenox, 1; Ludlow, 1; Mansfield, 1; Marblehead, 1; Mattapoisett, 1; Natick, 1; Northampton, 2; Northborough, 1; Palmer, 2; Pittsfield, 21; Quincy, 2; Reading, 1; Revere, 1; Richmond, 1; Rockport, 1; Sandwich, 1; Sharon, 1; Southbridge, 1; Springfield, 39; Stockbridge, 2; Waltham, 1; Watertown, 1; West Springfield, 5; Westfield, 1; Whitman, 2; Wilbraham, 1; Williamsburg, 1; Williamstown, 1; Winchester, 1; Worcester, 1; total, 137.

Diphtheria was reported from: Boston, 3; Lowell, 1; Medford, 1; New Bedford, 1; total, 6.

Dysentery, bacillary, was reported from: Boston, 2; Lawrence, 1; Malden, 1; Milton, 1; Salem, 4; Worcester, 1; Wrentham, 8; total, 18.

Encephalitis, infectious, was reported from: Braintree, 1; total, 1.

Malaria was reported from: Boston, 4; Cambridge, 1; Camp Edwards, 15; Cushing General Hospital, 25; Lawrence, 1; Merrimac, 1; Somerville, 1; Springfield, 1; Weymouth, 1; Woburn, 1; total, 49.

Meningitis, meningococcal, was reported from: Agawam, 1; Beverly, 2; Boston, 14; Bourne, 1; Brockton, 2; Chicopee, 1; Dartmouth, 1; Gardner, 1; Lynn, 2; Somerville, 1; Springfield, 1; Sutton, 1; Swampscott, 1; Watertown, 1; Westfield, 1; West Bridgewater, 1; West Springfield, 1; Worcester, 1; total, 34.

Meningitis, Pfeiffer-bacillus, was reported from: Boston, 1; Cheshire, 1; Hampden, 1; total, 3.

Meningitis, pneumococcal, was reported from: Agawam, 1; total, 1.

Meningitis, undetermined, was reported from: Boston, 1; Rehoboth, 1; total, 2.

Rocky Mountain spotted fever was reported from: Chatham, 1; total, 1.

Salmonella infections were reported from: Attleboro, 1; Beverly, 2; Boston, 3; Lawrence, 3; Lynn, 1; Manchester, 1; Marblehead, 1; Melrose, 2; Needham, 1; Newton, 2; North Andover, 3; Rehoboth, 1; Springfield, 1; Worcester, 2; total, 24.

Septic sore throat was reported from: Boston, 1; total, 1.

Trichinosis was reported from: New Bedford, 1; total, 1.

Typhoid fever was reported from: Boston, 3; Charlton, 1; Worcester, 1; total, 5.

Undulant fever was reported from: Beverly, 1; Conway, 1; Falmouth, 1; Grafton, 1; Medway, 1; Norfolk, 1; Rutland, 1; total, 7.

Weil's Disease was reported from: Medford, 1; total, 1.

CORRESPONDENCE

ALKALINIZATION DURING SULFONAMIDE THERAPY

To the Editor: I was both surprised and pleased to read the editorial "Alkalinization During Sulfonamide Therapy," which appeared in the September 14 issue of the *Journal*.

The author of this excellent editorial, I believe, is correct in pointing out that the key problem to be solved, before the use of potassium bicarbonate is given widespread acceptance, is not its rationale, for that is obvious, but rather the toxicity of potassium bicarbonate when given in the large doses necessary to achieve adequate urinary alkalinization (18 to 22 gm. on the first day and 12 to 15 gm. on succeeding days). We have not seen any toxic effects either in the cases reported in our paper or since then, but it is true that our

experience has been relatively small. From our review of the literature it seemed that potassium retention was only seen in really terminal uremia; the other situation under which potassium toxicity might be expected — untreated Addison's disease coexistent with congestive heart failure — is a metabolic paradox and rare enough to be considered a medical curiosity. It must be admitted, however, that this point of view is not shared by all; thus, Dr. Paul D. White in the 1944 edition of his book *Heart Disease* states, "Calcium (and potassium) salts in high dosage should not be administered to digitalized patients because of the hazard of serious toxic effects on the cardiac mechanism."

Although further demonstration of the harmlessness of potassium salts is desirable, I do not believe that the suggestion advanced by the author of the editorial to avoid possible toxicity is practicable. He suggests the use of smaller doses (5 to 10 gm. daily) of potassium bicarbonate; but, unfortunately, although this might eliminate the possibility of toxicity, it would probably also abolish the beneficial therapeutic effect. The reason for this is to be found in the solubility curves of sulfadiazine and acetyl-sulfadiazine, which only begin to rise rapidly as the alkalinity of the urine approaches pH 7.4. I am afraid that 5 to 10 gm. daily would not often serve to render the urine alkaline enough to achieve the desired effect.

Although we believe that our dosage schedule is not likely to cause toxicity, I should like to suggest that instead of using smaller dosages of potassium bicarbonate alone, those who fear potassium bicarbonate toxicity use a mixture of potassium bicarbonate and sodium bicarbonate. If 10 gm. of potassium bicarbonate and 4 gm. of sodium bicarbonate are given daily, one would be within the generally accepted limits of safe potassium dosage and would also be able to achieve satisfactory alkalinization without giving more sodium than is contained in the ordinary hospital salt-poor diet. This is, of course, only a makeshift at best and should be abandoned if the concept of the low toxicity of potassium salts becomes established.

WILLIAM QUITMAN WOLFSON, M.D.

Greenpoint Hospital
Brooklyn 6, New York

A COMMUNITY BLOOD BANK

To the Editor: The editorial in the August 17 issue of the *Journal* pertaining to "Red-Cell Residues" is most excellent, commendable and timely. In the concluding sentences of the last paragraph, it reads: "One might think of each community with a blood-donor service prepared to supply whole blood, plasma, albumin, specific globulin fractions and erythrocyte suspensions. The proper use of such a service would require the co-operation of the physicians within the community, but the therapeutic possibilities are manifold."

May I call to your attention the fact that the Worcester District Medical Society has already established the type of service that the editorial portrays as a pious hope for the future. The Worcester blood bank, officially named the Worcester District Community Center for Aiding Transfusions, Incorporated, is sponsored by the Worcester District Medical Society and began its service to this community on October 12, 1942. It has given whole blood, plasma, erythrocyte suspensions and erythrocyte packs to any physician or hospital for the asking. In addition, we are serving the Lovell General Hospital at Fort Devens.

The cost of preparing this material is one of the lowest in the country, volunteer workers numbering over two hundred and only four full-time paid workers helping to keep the costs down. The expense of this service is supported in part by the patients receiving the material and in part by the Community Chest of Worcester.

This program is actual proof that a community without governmental help can successfully offer inexpensive community service. Furthermore, it can be said with emphasis that no one in the Worcester District has suffered from the lack of whole blood or blood components since this blood bank began its operations.

We believe that it is worth while to call this matter to your attention so that physicians in other communities can study the possibilities of community service without governmental dole.

WILLIAM FREEMAN, M.D., Secretary

57 Cedar Street
Worcester, Massachusetts

BOOK REVIEWS

Roentgenographic Technique: A manual for physicians, students and technicians. By Darmon A. Rhinehart, M.D. 8°, cloth, 471 pp., with 201 illustrations. Philadelphia: Lea and Febiger, 1943. \$5.50.

A careful reading of this book indicates, in the opinion of the reviewer, that the technic proposed by this writer is the one that was in use a decade ago. It gives practically no information to the radiologist or technician in a large hospital for special work referable to the skull, such as encephalography and ventriculography, which are frequently employed.

Nervousness, Indigestion, and Pain. By Walter C. Alvarez, M.D. 8°, cloth, 488 pp. New York: Paul B. Hoeber, Incorporated, 1943. \$5.00.

The author, primarily a gastroenterologist, has long been interested in the nervous manifestations of diseases, particularly the resulting dysfunctions in the gastrointestinal tract. The book is the result of his long experience and is a personal report on what he has seen and recorded. He is thus in a position to evaluate many puzzling problems regarding one of the most complicated types of illness facing the general practitioner.

The book is full of sound advice, particular emphasis being placed on the diagnosis of disease from a complete history and physical examination from extensive laboratory data. The problems of constitutional inadequacy, nervous breakdowns and the menopause as well as many other topics, are handled with great skill. In reading the book one feels as though the author and his patient were in the same room and one was actually attending as an observer. The reviewer knows of no other book that so distinctively gives this impression. No one can read this book without being a better physician, and in it will be found the answer to many problems that have long been a trying annoyance to many practitioners. The various subheadings of the chapters give the tone of the book: "We, physicians, are giving our patients the impression that we diagnose only from laboratory reports"; "It is hard to take a good history without revealing one's knowledge as to the diagnosis"; "It is good to be somewhat neurotic"; "Nothing could be found at operation"; "The qualities desirable in the physician"; "Dilemmas that result from lying"; "Abdominal hallucinations"; "The woman who revels in medical treatment"; "The schoolteacher who tries every summer to get a master's degree"; and "What is the patient to do?"

This book is highly recommended.

Lincoln-Douglas: The weather as destiny. By William F. Petersen, M.D. 8°, cloth, 211 pp., with 16 illustrations. Springfield, Illinois: Charles C Thomas, 1943. \$3.00.

The author has long been interested in the effects of cosmic disturbances on disease. He has written a number of books on the weather and its relation to epidemics and even to individual disease. In this volume he contrasts the environments under which Lincoln and Douglas were raised and developed. Their backgrounds were essentially dissimilar, Douglas being raised in Vermont in a prosperous family, the mother being in excellent health, and the other born under depressed circumstances in a log cabin, his mother being ill and probably suffering from tuberculosis. The body build of the two men was also distinctly in contrast, Douglas was short, rotund, broadchested, with square shoulders, small hands and feet, and of a buoyant, energetic, bustling personality; Lincoln, on the other hand, was excessively tall, stoop-shouldered, gaunt and awkward, with a shrill, squeaking voice. With these data the author investigates the weather conditions during the life of the individuals and attempts to correlate the influence that these had on the career of the two men.

The theory seems strained to meet requirements, and the book is not entirely convincing. The volume, however, is of interest to the medical profession for it deals with a topic much in current discussion. How much stress should be put upon weather as an effective agent in individual destiny is, to most scientists, an unanswered problem. The author believes that it plays an important role, even an outstanding one.

NOTICES

JOSEPH H. PRATT
DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday, October 6 — War Neuroses and Their Treatment in the Army. Major Jackson Thomas, U.S.A.

Wednesday, October 11 — Headaches Due to Ocular Disorders. Dr. Joseph J. Skirball.

Friday, October 13 — Deep Burns and Prophylactic Penicillin. Dr. Oliver Cope.

Wednesday, October 18 — Problems in Rhinology. Dr. Daniel Miller.

Friday, October 20 — Precordial Electrocardiography. Dr. Conger Williams.

Wednesday, October 25 — Pyuria in Children. Dr. James Marvin Baty.

Friday, October 27 — The Diagnostic Significance of Change in the Appearance of the Tongue. Dr. H. J. Jeghers.

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases.

On Saturday mornings clinics will be given by Dr. William Dameshek.

NEW ENGLAND DERMATOLOGICAL
SOCIETY

Because of the holiday on October 12, the next regular meeting of the New England Dermatological Society will be held in the Skin Out Patient Department of the Massachusetts General Hospital on Wednesday, October 18, at 2 p. m.

NEW ENGLAND OTO-LARYNGOLOGICAL
SOCIETY

The regular fall meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary on Wednesday, November 15.

METROPOLITAN STATE HOSPITAL

The tenth Postgraduate Seminar in Neurology and Psychiatry will begin Wednesday, October 11, at the Metropolitan State Hospital, 475 Trapelo Road, Waltham. The program consists of fifty-four lectures and demonstrations in anatomy, applied physiology, pathology and roentgenology of the nervous system, clinical neurology and psychiatry. The lectures will be held every Wednesday from October 11 through December 13 and from January 3 through April 25, from 6 to 10 p. m. The seminar is open to all graduate physicians. Those interested are requested to register October 11 at 5:30 p. m. at the Metropolitan State Hospital.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING
THURSDAY, OCTOBER 12

SATURDAY, OCTOBER 14
*10:00-11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, OCTOBER 16
*12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 17
*12:15-1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, OCTOBER 18
*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

OCTOBER 6-27. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Notice elsewhere on this page.

OCTOBER 9-20. 1944 Graduate Fortnight of the New York Academy of Medicine. Page xvii, issue of July 27.

OCTOBER 10. New England Society of Anesthesiology. Page xvii, issue of September 7.

(Notices continued on page xv)

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Number 15

TREATMENT OF MENINGOCOCCAL MENINGITIS WITH PENICILLIN*

MANSON MEADS, M.D.,† H. WILLIAM HARRIS, M.D.,‡ BERNARDO A. SAMPER, M.D.,§
AND MAXWELL FINLAND, M.D.¶

WITH THE TECHNICAL ASSISTANCE OF CLARE WILCOX

BOSTON

IN SOME of his early studies on penicillin, Fleming¹ reported that meningococci and gonococci are among the bacteria that are highly sensitive to penicillin in vitro and that they rank with staphylococci in this respect. This observation has been confirmed by others,²⁻⁴ but few strains were tested in each instance. Dawson and his co-workers⁵ showed, in addition, that penicillin is effective against experimental Group I meningococcal infection in mice. A total dose of 1800 Oxford units given subcutaneously in sesame oil a half, eighteen and twenty-four hours after intraperitoneal injection of organisms afforded complete protection against 10^{-5} and 10^{-6} dilutions of meningococci, and partial protection against 10^{-3} and 10^{-4} dilutions. These amounts of each of two cultures tested were fatal to control mice in twenty-four hours.

Clinical applications of these findings, as they concern the gonococcus, have been many,⁶⁻¹² but they have been chiefly confined to the treatment of sulfonamide-resistant gonorrhea, which almost invariably responds to penicillin in adequate doses. On the other hand, because of the good results obtained with sulfonamides, extremely few cases of meningococcal infections treated with penicillin have been reported. Keefer's¹³ series included 5 cases with 1 death. In the fatal case and one other the patient received only parenteral and no intrathecal therapy. Dawson and Hobby¹⁴ reported 2 cases of

meningitis; in one, both intrathecal and intramuscular penicillin were given after the patient developed anuria as a result of sulfonamide therapy; in the other, the patient, a seventeen-month-old baby, was given only intramuscular penicillin. The former recovered, and the authors believed that recovery was attributable to the penicillin. The latter made an unsatisfactory response to the penicillin and subsequently responded to antimeningococcus serum and sulfonamide therapy. Both groups of workers concluded that intrathecal as well as parenteral therapy with penicillin is probably necessary to obtain good results. Lyons¹⁵ reported the case of a successfully treated patient with meningococcemia without meningitis who had presumably relapsed after sulfonamide therapy. The War Department⁸ recommends penicillin therapy for meningococcal infections only if sulfadiazine cannot be given or if there is a failure to respond to that drug in forty-eight hours. For fulminating cases with bacteremia, collapse and purpura, it is recommended that both penicillin and sulfadiazine be given at the earliest practicable time.

In this paper are presented 9 cases of meningococcal meningitis, including 5 with meningococcemia, that were treated with the calcium salt of penicillin intrathecally and intramuscularly. The reason for presenting such a small series of cases in some detail will become evident from the character of the clinical response that was obtained.

CASES AND METHODS OF STUDY

The cases studied were unselected typical ones of meningococcal meningitis admitted to the Boston City Hospital during April, 1944. The ages ranged from fourteen to fifty-eight years. Seven patients were acutely ill and irrational, 1 was acutely ill and rational, and 1 was only moderately ill when first seen. The duration of the acute illness before entry ranged from one to seven days, averaging about three days. Two of the patients were alcoholic

*From the Medical Laboratory, Second and Fourth City Hospital, and the Department of Medicine.

†The penicillin used in this study was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutic and Other Agents of the National Research Council.

‡Presented in part at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

§Research fellow, Thorndike Memorial Laboratory, Boston City Hospital, and Harvard Medical School.

¶Research fellow, Thorndike Memorial Laboratory, Boston City Hospital.

§Formerly, research fellow, Thorndike Memorial Laboratory, Boston City Hospital, and Harvard Medical School.

¶Assistant professor of medicine, Harvard Medical School, chief, Fourth Medical Service, and associate physician, Thorndike Memorial Laboratory, Boston City Hospital.

addicts, and 4 gave histories of their illness as starting with an acute upper respiratory infection. Blood for sulfonamide determination was taken routinely on admission to ascertain whether therapy with these drugs had been given before entry. No sulfonamide was found except in Case 9, in which the blood level was 2.4 mg. per 100 cc., calculated as free sulfadiazine. It was later learned that this patient had received an oral dose a few hours before entry. Lumbar punctures were done on admission and at twelve-hour to twenty-four-hour intervals, as will be indicated later. Cell counts, smears and cultures of the sediment and chemical studies of the cerebrospinal fluid were carried out routinely. Blood and throat cultures were made on admission and, in some cases, were repeated once or twice daily until they were negative.

Cultures of the spinal-fluid sediment obtained by high-speed centrifugation were made on the surface of 10 per cent horse-blood-agar plates and also in beef infusion broth containing 1 per cent horse blood. Incubation was carried out at 37.5°C. in a candle jar. The time elapsing between lumbar tap and culture was kept as short as possible in order to minimize the penicillin inhibition. In several cases spinal fluid for culture was taken both before and after withdrawing 10 to 15 cc. of fluid, but this did not result in a higher percentage of positive cultures. Identification of the meningococcus was carried out by gram-stained smears of the sediment and by typing. If moderate numbers of gram-negative diplococci were seen, direct typing by capsular swelling¹⁶ was attempted; otherwise, typing was done from the blood-broth culture on the following day.

Treatment

All cases were started on both intramuscular and intraspinal penicillin immediately after the diagnosis was made.

Intraspinal therapy. Initial intraspinal doses consisted of 10,000 to 20,000 units in 10 cc. of sterile physiologic saline solution, to replace a similar or larger volume of spinal fluid withdrawn. The spinal-fluid dynamics were tested before each dose was given to be sure that no block was present. From 5000 to 15,000 units of penicillin was then given intraspinally at twelve-hour intervals for two to five doses and every twenty-four hours after improvement was noted bacteriologically and clinically, and this dosage was continued until clinical and bacteriologic recovery took place. In some cases, the twelve-hour regime was resumed because of the poor clinical response and the persistence or recurrence of abnormal spinal-fluid findings. The number of intraspinal injections given each patient varied from three to eleven, averaging about six, and the total amount of penicillin given intrathecally varied from 30,000 to 150,000 units, averaging about 75,000 units.

Intramuscular therapy. Doses of 15,000 units were given intramuscularly every three hours in 7 cases and doses of 10,000 units every three hours in 2 cases. This therapy was continued until there were signs of definite clinical improvement. The duration of intramuscular therapy was two and a half to six and a half days. The total amount of penicillin given in each case by this route ranged from 190,000 to 1,155,000 units, averaging almost 500,000 units. In Case 7 on the thirteenth day and in Case 8 on the fourth day, because of poor clinical response and persistence of abnormal bacteriologic and spinal-fluid chemical findings, penicillin was discontinued and sulfapyrazine was given, first parenterally and then orally in standard doses. Case 1, because of persistent positive throat cultures after one week of penicillin therapy, a four to eight-hour course of sulfadiazine was given orally. No other specific therapy was used.

RESULTS

The relevant findings in the 9 cases are summarized in Table 1 and in the accompanying charts (Figs. 1-7). In all cases except Case 9, a Group I meningococcus was isolated from the spinal-fluid sediment, and in 5 cases the same organism was

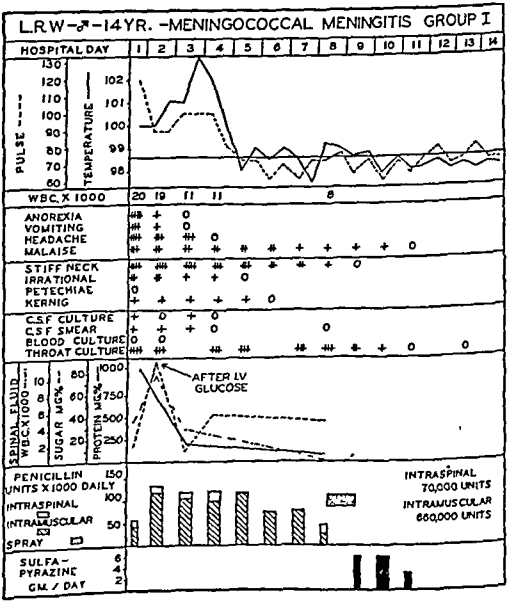


FIGURE 1. Case 1.

In this patient the meningeal infection was not controlled bacteriologically or symptomatically until after the fourth day of penicillin therapy. Nasopharyngeal cultures still yielded copious growth of Group I meningococci after a week of intramuscular and intrathecal therapy and after frequent spraying of the nose and throat with a penicillin solution for twenty-four hours. Negative cultures were obtained after one day of sulfonamide therapy.

covered from blood cultures. In 4 of 7 patients in whom nose and throat cultures were made, a Group I meningococcus was also isolated from the na-

harynx. One patient (Case 9) who had received a single oral dose of sulfadiazine before entry had negative spinal-fluid and pharyngeal cultures, even though para-aminobenzoic acid had been added to the culture medium.¹⁷

Clinical Response

In 6 cases, improvement was first observed in one to five days after treatment was started, averaging

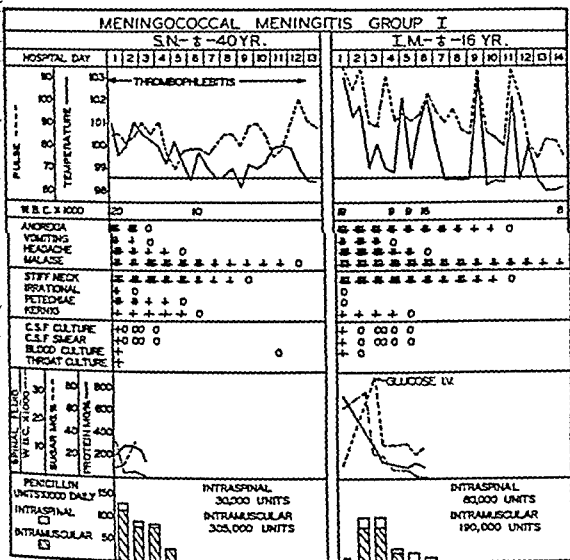


FIGURE 2. Case 5 (left) and Case 2 (right). Each patient showed a prompt bacteriologic response to intramuscular and intrathecal penicillin therapy, but the fever and symptoms persisted for several days.

about three days, as shown in Table 1 and Figures 1 to 5. In Case 7 (Fig. 6) there was a clinical recurrence on the twelfth day, and in Case 8 (Fig. 7) one on the fourth day. The clinical course did not justify continuance of penicillin therapy in these cases and sulfapyrazine was substituted. Response to the sulfonamide therapy was striking and occurred within twelve to thirty-six hours. In Case 9 (Fig. 5), in which sulfonamide therapy had been given before admission, the patient responded favorably after twenty-four hours of penicillin treatment.

The 6 patients treated only with penicillin became afebrile in five to fifteen days, the average being almost ten days. In Case 9, the fever lasted only three and a half days, which was less than in any other case in the series. In Case 7 it continued for only twenty-four hours after sulfonamide therapy was started, and in Case 8 for fifty-two hours.

Bacteriologic Response

Spinal fluid. In 2 of the 8 cases with positive cultures before treatment, the meningococcus could not be cultured at the time of the second lumbar puncture twelve hours after the start of therapy. In 4 cases, cultures of the cerebrospinal fluid re-

mained positive for twenty-four to sixty hours. In Case 7, the culture was positive after twelve hours, and later specimens showed gram-negative diplococci on smear on the fourth and seventh days, along with a recurrence of abnormal chemical findings. Growth in cultures was then obtained on the twelfth and thirteenth days. In Case 8, the last time growth of meningococci was obtained was after twelve hours, but positive smears were found after ninety hours.

Blood. In all 5 patients with positive blood cultures on admission, all subsequent cultures were negative. The second blood culture was always taken ten to twelve hours after the start of therapy.

Throat. Repeated throat cultures were made in 2 of the patients whose initial cultures were positive. The last positive culture in one of them (Case 8) was obtained after three days, and in the other (Case 1) after seven and a half days of intramuscular penicillin (660,000 units). In the latter, the culture was still positive after twenty-four hours of throat and nose spray with penicillin (400 units per cubic centimeter every two hours during the day and three times at night). In both the patients, the throat cultures became negative for meningococci within forty-eight hours after sulfadiazine was given orally in therapeutic doses.

Clinical and Cytologic Response of Spinal Fluid

As evaluated by the protein and sugar levels and the number of cells and their differential count,

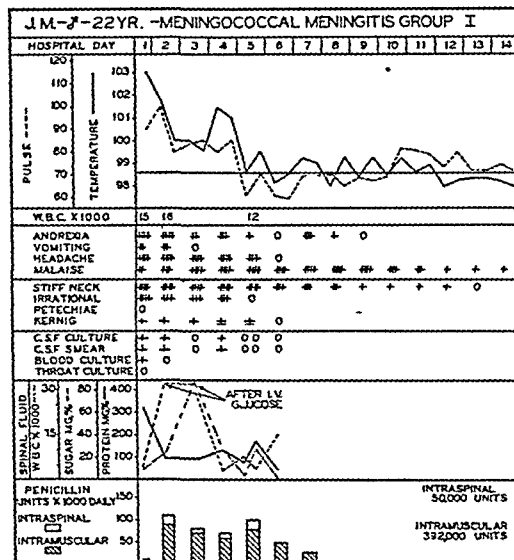


FIGURE 3. Case 3.

Cultures of the cerebrospinal fluid in this patient did not become negative until the fifth day of intramuscular and intrathecal penicillin therapy. During that time the patient continued to be irrational; he improved slowly thereafter.

the spinal-fluid findings returned approximately to normal in two and a half to eight days, with an average of five and a half days.

Complications

No complications occurred that could be attributed to the calcium salt of penicillin except possibly a scarlatiniform rash that appeared in 1 case on the fourth day of penicillin therapy. It is possible, however, that this rash was a result of erythro-

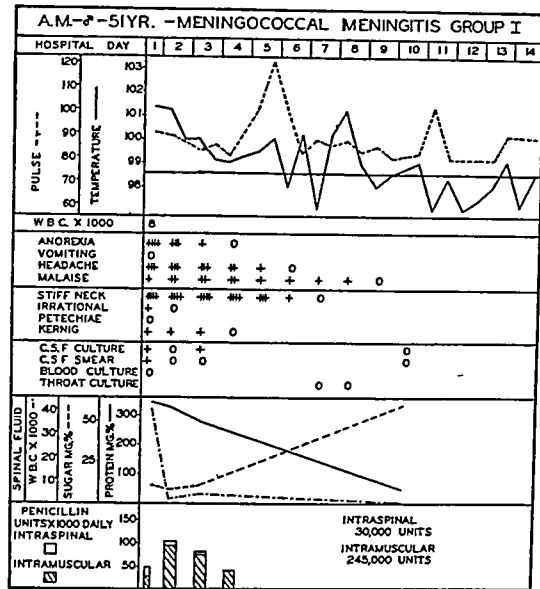


FIGURE 4. Case 4.

In this case, cultures of the spinal fluid were still positive on the third day. The patient was definitely improved after twenty-four hours but continued to have some meningeal symptoms for several days.

toxins derived from extensive herpes lesions that were secondarily infected with *Staphylococcus aureus* at the time of onset of the rash. In Case 5, there was a thrombophlebitis on entry, which became worse on the third hospital day and persisted through the twelfth day. One patient (Case 6) had a convulsion eight hours after the first intrathecal injection. This was probably due to increased cerebrospinal-fluid pressure, which may have resulted from the penicillin injection.¹⁸ In Case 7, there developed signs of consolidation of the left lower lobe, and many Type 8 pneumococci were identified in the sputum thirty-six hours after the intramuscular penicillin therapy was stopped. This complication failed to respond clinically or bacteriologically to doses of 15,000 units of penicillin given intramuscularly every three hours for forty-eight hours. One patient (Case 9) developed arthritis of the right knee on the third hospital day; on the ninth day, this was tapped and culture of the fluid was sterile.

Tests for Sensitivity of Strains

The strains of meningococcus recovered from 5 patients in the present series were tested for sensitivity to penicillin according to the method used by Rammelkamp and Maxon.¹⁹ One strain was

completely inhibited by 1.25 units per cubic centimeter, 3 by 0.625 units, and 1 by 0.312 units. The latter was obtained from Case 1, and the organism obtained after one week of penicillin therapy in this case was also tested and showed no increase in its resistance. This range of sensitivity puts these particular strains in a category with the more resistant strains of *Staph. aureus* and *Streptococcus viridans*.

All five strains failed to grow in peptone-fructose synthetic media containing 1 mg. per 100 cc. of sulfadiazine. This may be taken as an indication of the great sensitivity of these strains to sulfadiazine in vitro.

Penicillin Levels

Spinal-fluid levels of penicillin, tested by the Rammelkamp and Maxon¹⁹ method of serial dilution against a stock strain of streptococcus, varied within wide limits. They showed that the level

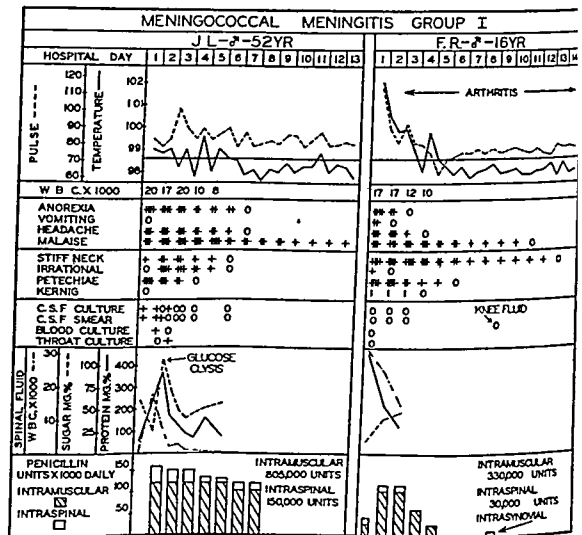


FIGURE 5. Case 6 (left) and Case 9 (right).

In Case 6 the patient continued to have positive blood cultures (Group I meningococci) for twelve hours and positive spinal-fluid cultures for thirty-six hours after intensive intramuscular and intrathecal penicillin therapy. He remained acutely ill for about five days, after which he steadily improved. In Case 9, the clinical features were characteristic of cerebrospinal fever but all cultures and smears taken on admission were negative for meningococci. It was later learned that this patient had received a single dose (2 gm.) of sulfadiazine shortly before being sent to the hospital, and blood taken on admission showed a free sulfadiazine level of 2.4 mg. per 100 cc. Definite clinical improvement occurred within twelve hours and continued steadily thereafter.

obtained in the lumbar canal eight to twelve hours after intraspinal injections were more than adequate for bacteriostasis.

COMMENT

Smith et al.²⁰ reported 43 cases of meningococcal meningitis treated with sulfonamides. Twenty were Group I infections, and 5 of these patients died. In 14 cases in which the clinical response could be

evaluated, the average time between the initial dose of sulfonamide and clinical improvement was one day. Fever persisted for an average of five and a half days after the onset of treatment. In 11 cases, negative cerebrospinal-fluid cultures were

a mortality of 3.1 per cent, and Appelbaum and Nelson²¹ reported a 1.4 per cent mortality in 141 consecutive cases treated with sulfadiazine and its sodium salt.

The results in the 8 cases reported here in which no sulfonamide therapy had been given previous to admission show clearly the poor clinical and bacteriologic response to calcium penicillin obtained in cases of Group I meningococcus meningitis as compared with sulfonamide-treated cases. In this series, it is impossible to evaluate the effect of the intraspinal therapy in relation to the severity of infection on admission and to the duration of illness before treatment. From bacteriologic sensitivity tests and from observed spinal-fluid penicillin levels, it can be assumed that many more times the bacteriostatic level of penicillin was obtained for at least twelve hours after its installation in the lumbar canal. The most probable explanation offered at present is, first, the failure of penicillin to penetrate to any significant extent into the cerebrospinal fluid from intramuscular or intravenous administration, and second, the failure to obtain a proper distribution of penicillin throughout the cerebrospinal fluid after intraspinal injection, thus preventing contact of the drug with many of the organisms. This may serve to explain the per-

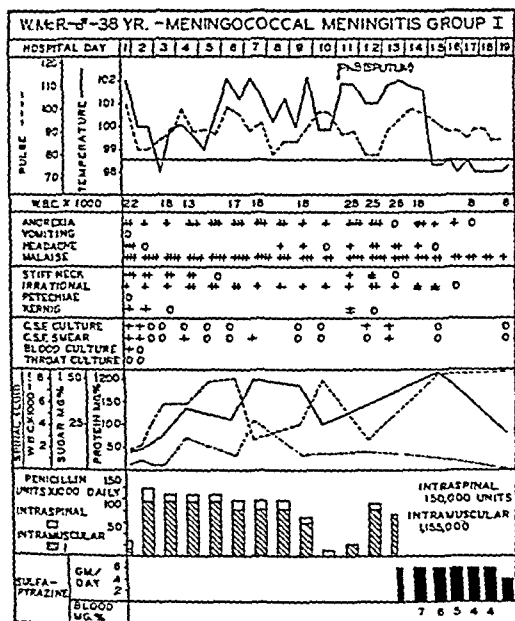


FIGURE 6. Case 7.

In this patient the infection was not controlled clinically or bacteriologically after nine days of intensive intrathecal and intramuscular penicillin therapy. On the second day after intramuscular injections were discontinued, the patient developed lobar pneumonia of the left lower lobe and a copious growth of Type 8 pneumococci was obtained from the sputum. Resumption of penicillin therapy failed to control either the meningeal or the pulmonary infection. Clinical improvement began within a few hours after sulfonamide therapy was started, and the patient had essentially recovered thirty-six hours later.

obtained twelve to eighteen hours after the start of therapy and in the remaining 3 the cultures were positive for seventeen to twenty-four hours. Banks²¹ in a series of 72 cases treated with sulfanilamide and M. & B. 693 without antiserum noted that the acute symptoms disappeared rapidly and the temperature in most cases returned to normal in two to six days. In 66 patients the spinal fluid was sterile in twelve to twenty-four hours and in 4 it became sterile in twenty-four to forty-eight hours; only 1 patient was found to have a positive fluid after forty-eight hours. Spinal-fluid cell counts fell to below 500 in three or four days, and 90 per cent of the cells were mononuclears in five to six days.

The efficacy of the sulfonamides has been shown in a review of mortality rates by Dingle and Finland.²² In over 1000 cases treated with sulfanilamide there was a mortality rate of 1.4 per cent; in 700 cases treated with sulfapyridine and 26 treated with sulfathiazole it was 8 per cent. Recently, in a series of 129 sulfadiazine-treated cases of meningococcal meningitis, Marangoni and D'Agati²³ reported

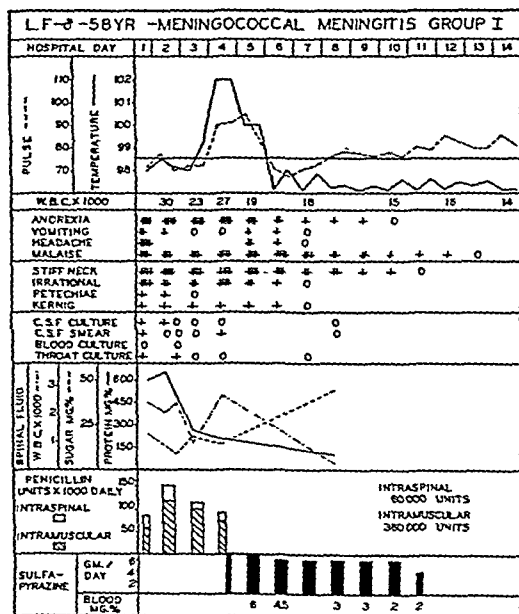


FIGURE 7. Case 8.

This patient remained acutely ill and irrational during four days of therapy with penicillin intrathecally and intramuscularly. Because he was obviously getting worse clinically, sulfonamide therapy was then given. Improvement began within a few hours and steadily continued.

sistence of exudate and consequent pocketing-off of organisms, adhesion formation and pressure difficulties. The rapid and complete distribution of the

sulfonamides throughout the cerebrospinal fluid of six taps were done in addition to occasional unsuccessful ones. This factor makes management by post-mortem studies. This may explain the difficult as compared with sulfonamide administra-

TABLE 1. *Summary of Clinical and Bacteriologic Findings in Nine Cases of Meningococcal Meningitis Treated with Calcium Penicillin.*

CASE No.	AGE	SEX	DURA- TION AT ENTRY	PREDIS- POSING FACTORS	SEVER- ITY AT ENTRY*	INITIAL BACTERIOLOGIC FINDINGS†				PENICILLIN TREATMENT						
						CEREBROSPINAL FLUID Culture	BLOOD Smear	BLOOD CUL- TURE	THROAT CUL- TURE	INTRAMUSCULAR			INTRASPINAL			Total Doseage units × 10 ³
										3-hour Dose units × 10 ³	Duration days	Total Dosage units × 10 ³	Single Dose units × 10 ³	Inter- val hr.	No. of Doses	
	yr.		days													
1	14	M	2-3	Upper respiratory infection (3-4 days)	+++	+	+	0	+	15 10	6 1½	660	15 10 15 15	12 24 24 120	2 1 1 1	70
2	16	F	1½	0	++	+	+	+	-	10	2¼	190	10 10 10	12 24 12	4 2 2	80
3	22	M	3	0	+++	+	+	+	0	10	5½	392	10 10 10	12 24 12	3 1 2	60
4	51	M	2	Upper respiratory infection 7 days; chronic alcoholism	+++	+	+	0	-	15 10	½ 2	245	15 10 5	Stat. 12 24	1 1 1	30
5	40	F	3	Upper respiratory infection (7 days)	+++	+	+	+	+	15 10	½ 2½	305	10 5 5	Stat. 12 24	1 3 1	30
6	52	M	1	0	+	+	+	+	+	15	6½	805	20 15 15 10 15	Stat. 12 24 24 24	1 5 1 1 2	150
7	38	M	7	Chronic alcoholism	+++	+	+	+	0	15 0 15	7½ 4 2	1,155	15 15 10 10 10	12 24 36 24 36	4 4 1 1 1	150
8	58	M	3	0	+++	+	+	0	+	15	3	360	15 10 10 15	Stat. 12 24 24	1 2 1 1	60
9	16	M	2	Upper respiratory infection (7 days)	+++	0	0	0	0	15 10	2 1	330	10 10	12 24	2 1	30

*+++ = acutely ill, irrational; ++ = acutely ill, rational; and + = moderately ill.

much more favorable clinical and bacteriologic response to the sulfonamides.

In these patients the number of lumbar punctures in each case varied from three to eleven. An average

tion, in which often a single diagnostic puncture is all that is necessary.

Meningococcemia, on the other hand, seemed to respond rapidly. The persistence of positive throat

cultures in one case for four days and in another until sulfadiazine was given on the ninth day reveals another possible disadvantage of penicillin therapy.

fections. Cheever et al.²⁵ in a study of 161 cases of meningococcal infections of the nasopharynx showed that nasopharyngeal cultures became negative for

TABLE 1 (Continued).

Case No	RESPONSE TO PENICILLIN THERAPY						COMMENTS, COMPLICATIONS AND SO FORTH
	Cerebrospinal Fluid Culture	BACTERIOLOGIC† Smear	Blood Culture	Throat Culture	CLINICAL‡ Definite Improvement days	Afebrile days	
	38 hr 62 hr	38 hr 62 hr	0	9 days 10 days	5	9	Penicillin by nose and throat spray for 24 hr. on 8th day, sulfadiazine from 9th to 11th day.
2	Admission 12 hr	Admission 12 hr	Admission 12 hr	—	4	12	
3	60 hr 84 hr	60 hr 84 hr.	Admission 12 hr	0	5	11	Extreme weakness, clinical and bacteriologic recurrence on 4th day
4	40 hr 9 days	Admission 12 hr	0	—	1	9	Scarlatinal rash from 4th to 8th day
5	Admission 12 hr	Admission 12 hr	Admission 12 hr	—	1	15	Thrombophlebitis on entry, patient worse on 3rd day, improved on 12th day
6	24 hr 36 hr	12 hr 18 hr	Admission 12 hr	12 hr	4	5	Convulsion 8 hr after first lumbar tap, patient looked worse and remained confused for 3 days in spite of improved spinal-fluid findings
7	15 days 15 days	15 days 15 days	Admission 10 hr	0	14	14	Lobar pneumonia (Type 8 pneumococcus) on 11th day — 36 hr after intramuscular penicillin stopped, three apparent clinical and bacteriologic relapses under penicillin therapy, complete recovery after sulfapyrazine in 36 hr
8	12 hr 24 hr	4 days 8 days	0	2 days 3 days	5	5	Patient given sulfapyrazine on 4th day because of increasing irritability and no improvement in spinal fluid findings, response to sulfapyrazine in 12 hr, serologic syphilis (blood and spinal fluid)
9			0		1½	3½	Arthritis in right knee 36 hr after entry (first tap, on 9th day, sterile), blood sulfadiazine on admission 2.4 mg per 100 cc (patient had received one oral dose 2 to 3 hr before entry)

†The numerator indicates time (at or after admission) of last positive culture, and the denominator the time of the first subsequent negative culture, 0 indicates that all cultures were negative, and — that no cultures were taken

‡The intervals represent the time after the first dose of penicillin

Adequate bacteriostatic levels of penicillin probably did not reach the nasopharynx in these cases. This certainly is another important consideration favoring the use of sulfonamides in meningococcal in-

meningococcus in all cases within seventy-two hours after a dose of 8 gm of sulfadiazine. This has now been adequately confirmed, even with smaller doses^{26, 27}

The possibility that the calcium penicillin used in the present cases was inferior in its therapeutic effects was considered. This seems unlikely for the following reasons. In vitro tests indicated full activity, in Oxford units, against standard strains of other bacteria. The same batch of calcium penicillin was given at the same time to a much larger number of patients with various other diseases, including cases of pneumococcal meningitis, with results comparable to those obtained with similar amounts of sodium penicillin. Intrathecal injection of the same lot in other subjects gave reactions that were actually slighter than those obtained with similar amounts of sodium penicillin. There were no local reactions from its use intramuscularly.

If good results are obtained from the treatment of meningococcal meningitis with penicillin, one must suspect that the patient has received sulfonamides before entry. He is not always in a condition to give a history of such therapy. The potent bacteriostatic effect of these drugs on the meningococcus is such that even one or two small oral doses may suffice to produce a complete bacteriologic and clinical response, as indicated by the experiences in the Anglo-Egyptian Sudan in 1938.^{28, 29} This was probably the factor that contributed to the rapid and favorable response observed in Case 9.

A comparison of the results of therapeutic studies on meningococcal infections in mice lends further support to the greater effectiveness of sulfadiazine *in vivo*. Thus, in contrast to the 1800 Oxford units used by Dawson et al.,⁵ as mentioned at the beginning of this paper, Thomas and Dingle³⁰ protected mice against similar infections with ten to ten thousand times the 50 per cent lethal dose of a virulent Group I meningococcus by giving only a single dose of 0.0025 mg. of sulfadiazine. For the average adult patient, these doses are equivalent, weight for weight, to about 10 mg. of sulfadiazine and 7,200,000 units of penicillin. The two studies are not entirely comparable, but the figures are certainly impressive when considered together.

Lastly, the finding in five consecutive cases of strains of meningococcus that are relatively resistant to penicillin seems to be in marked contrast to the results reported by others. Great differences in susceptibility to penicillin must occur and should be further investigated. These findings may explain, in part, the poor results obtained in this series.

CONCLUSIONS

The clinical and laboratory findings in this series of 9 cases of meningococcal meningitis treated with calcium penicillin, when viewed in the light of the accumulated results of sulfonamide therapy, suggest that the sulfonamides are the drugs of choice in the treatment of Group I meningococcus meningitis, and that penicillin may be effective in Group I meningococcus meningitis in the doses used, but

that the response is less favorable than that from sulfonamide therapy.

If penicillin is used, careful observations should be made of the clinical course, the spinal-fluid and nasopharyngeal bacteriology and the spinal-fluid chemistry.

The clinical response to penicillin is slower than that to the sulfonamides; abnormal spinal-fluid chemical and bacteriological findings persist longer, there may be recurrences; the meningococcus-carrier state may persist; the treatment is difficult, and, finally, one may eventually have to resort to the sulfonamides for cure.

Calcium penicillin seems to be quite effective against Group I meningococcus bacteremia.

Strains of Group I meningococcus vary markedly in their susceptibility to penicillin. In this respect, the strains studied in the present series resembled the relatively resistant ones of *Staphylococcus aureus* and *Streptococcus viridans*.

Several significant papers bearing on the present subject have appeared since this one went to press. Miller and Foster^{31, 32} reported favorable responses in vitro and in experimental infections with meningococcus, but special methods were required for this purpose. Rosenberg and Arling³³ used sodium penicillin in the treatment of 71 cases of meningococcal meningitis and meningococcemia without meningitis and noted favorable clinical responses, but many of the bacteriologic responses were similar to those reported here. Their general method of treatment was similar to that used in this series except that more thorough drainage of the spinal fluid was done before each intrathecal injection of penicillin. The authors, however, do not mention how frequently sulfonamides were used in their cases, and no mention is made of any special effort to determine that point. Only in the single fatal case is it noted that the patient received both sodium sulfadiazine and penicillin. From observations in our clinic and from many reports in the literature, particularly the experience in the Sudan,^{28, 29} it is to be expected that a single dose (2 or 4 gm.) of a sulfonamide given by a medical officer in a dispensary at the time when the diagnosis is suspected would be adequate to bring about most of the beneficial results. Rosenberg and Sylvester³⁴ were able to recover penicillin from the spinal fluids of cases of meningitis in concentrations of 0.03 to 0.35 unit per cubic centimeter after intravenous or intramuscular injections of 20,000 to 40,000 units. If this is corroborated it may prove possible and desirable to eliminate intrathecal therapy in some cases of meningitis and thus to avoid one of the major objections to the use of penicillin in these cases. Actual experience in treatment of cases of meningitis with penicillin alone would not seem to bear out this expectation.

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ARE DOCTORS PEOPLE?*

ROGER I. LEE, M.D.

BOSTON

IN MANY of the folklores, the doctor, or rather his analogue or prototype, appears as being quite set apart from ordinary people. He is seen in many forms and guises. If there is a touch of the lower animal about the medicine man, there is more of the deity. There is more of the saint than the devil, but some of both. There is madness, witchcraft and chicanery, but there is a larger amount of wisdom, sanity and honesty.

Of course primitive people merely created out of their own composite experiences — emotions, desires, fears and joys — their own gods, devils, saints, medicine men and various other important figures in their daily lives. Once the pattern was roughly established, there was a strong tendency to continue the type. But each medicine man used his own imagination, his own personality, good or bad, his own experience and a few of his own tricks to alter the pattern somewhat.

Strong members of the community or tribe always attempted to use the medicine man for their selfish ends. Sometimes they succeeded, sometimes they lost, and sometimes there was a new medicine man. Likewise, strong men would find that at times the gods were wholly co-operative, as we may call it. If there were priests of one kind or another who divulged the pleasure or displeasure of the gods, the priests might be persuaded to make a somewhat different interpretation, or possibly the strong men might do their own interpreting and find it easier to head both the spiritual and the temporal organizations. This was rarely done in

the case of the chieftain and medicine man, but the union of the priest and medicine man sometimes happened.

No brew of medicine, however, no matter how cunningly concocted, even in the most favorable phase of the moon, or even if subjected to the loudest of incantations, can heal certain mortal wounds or cure certain mortal diseases. Nor can such a brew restore a lost limb, eyesight or hearing. Nor can it replenish the ravages of time, more particularly in those feats of prowess fostered by the gods and goddesses of war and love. Thus it often seemed the part of discretion, if not of wisdom, to leave the medicine man, so to speak, on his own. If his brews, medicines and incantations were not satisfactory, one could try the potions and performances of another medicine man, perhaps one in a near-by community, perhaps one in a distant community, who had a reputation for healing certain ailments, or perhaps an upstart competitor in the same community.

Well, has the situation changed very much fundamentally? Patients get dissatisfied and seek help in distant places now as they did in the days of medicine men, perhaps as far from Worcester as Boston, New York or Rochester, Minnesota.

The community gets about the sort of medical practice it really wants and creates. At times the doctor is better than the community deserves, but in a small community especially, the medicine man of old and the doctor of today are quite at the mercy of malicious gossip. Of course, it is true that whereas the doctor gets blamed for many circumstances and accidents over which he has no control, he is also praised for certain happy outcomes to

*An address given by the president of the Massachusetts Medical Society at the one hundred and fiftieth anniversary of the Worcester District Medical Society, Worcester, May 10, 1944

which he contributed nothing—even though the balance is favorable to the doctor. Such a situation is stupid and wholly harmful. In the more recent but still bygone days of the apprentice method of education of the doctor, the old doctor passed on to his apprentice the secrets and tricks of his practice. Those were the days of rugged individualism of the doctors. It was this type of family doctor who caught the imagination and acquired the affection of a grateful community. Perhaps his practice of medicine was not perfect. Perhaps only sometimes did he bring cure, but he always brought comfort, physical and mental, to the patient and his family. In the modern days of formal medical education, medicine is far, far better, but it is not now free and independent. It is less so than in the days of the family doctor. Unfortunately or fortunately, as you will, medicine is now under the profound influence of lay opinion and lay action. The controlling bodies of educational institutions are naturally largely composed of laymen, that is, so far as medicine is concerned. Furthermore, there is a further lay and, at times, political control of the funds of some of the state medical schools. Of course the situation varies, but the president of a state university has to spend much time defending his budget before legislative committees. Some of these legislators have extremely positive ideas in regard to education, including medical education. The rejoinder is obvious, namely, that the president of a privately endowed university spends his time in argument with possible benefactors instead of with state legislators; and benefactors, like legislators, have their prejudices. In other words, the community still creates the medicine man in the image and in the pattern that it conceives to be the kind that delivers the most effective brew.

Now, this concept is not entirely whimsical, because it was not so long ago that a health officer found himself in jail for having ventured to diagnose a case of bubonic plague. That part of the country would not admit the existence of plague, and that was that. Of course the disease was not plague, and the doctor got out of jail, but after all, it was a lay resort to coercion in an unpleasant dilemma. It was merely the old story in a new setting: the tribal chief was sterile and his favorite wife was pregnant. Medical truth in the early days bowed to social convention, and today sometimes has to give a nod if not to turn a deaf ear.

Leprosy is a terrible disease, and no one wants to catch it. Consequently, because you and I do not want to have it, in our lay capacities we permit the unfortunate victims of this disease to be segregated on lonely islands. Such is the law and the practice. The truth is that leprosy is not especially contagious. Such barbaric cruelty is unjustified by the known medical facts.

These illustrations could be multiplied many times, merely adding more evidence of the dominance of the community over the medicine man. But it is not solely the dominance and control of medicine by the community that I want to discuss. We must accept the fact that the community, from the days of folklore and the medicine man to the present, conceives the medicine man and the doctor as someone apart from the rest of the tribe or the rest of the community. In the old days the medicine man often lived apart, painted his face egregiously and wore extraordinary masks. As a part of his performance he went through grotesque gyrations and gymnastics. Within the memory of many listeners, doctors wore an affair called a "Prince Albert" or frock coat. Certainly doctors were then, even more than now, rugged individualists, and I cannot visualize a convention of doctors setting up the Prince Albert coat as a sort of uniform for the profession. Consciously or not, the wearing of it was a dictum from the community. And take the gold-headed cane of another era. I have always maintained that the only practical use of the gold head was for the physician in those days to thrust it into his mouth to prevent his making any more of an ass of himself than he had already.

An erstwhile intern of mine in another city replied to my remark that because he drove such a luxurious car he could not be doing so badly financially. "In this city, patients will not go to a doctor who drives a Ford. I know because I tried it, and all my good friends and good patients spoke to me about it." I was about to make some remark more emphatic than polite about that city and state when it occurred to me that I had intended to ask him how he liked his office in an office building, since I was considering moving my office to a similar building in Boston. Such a building had, at first anyway, to be within a very restricted area—just the opposite of course, to the red-light district in character but really having the same implications. Of course, if one is famous like the Mayos, it makes no difference where one's office is. I know a doctor who receives his patients in bathing suits on the sand under a sun umbrella, but the locality is Palm Beach, and the doctor is a neuropsychiatrist.

Not long ago, a United States senator telegraphed that twenty doctors were needed at once for a war-boom town in his state. By the time the "sob sisters" in New York City got through with the story, it was two hundred doctors. There was no information about the kind of doctor wanted. It turned out that probably two doctors were required for a manufacturing plant—one a general practitioner and the other a physician with some knowledge of industrial medicine. The plant had been running for several months, and although its operator had not forgotten about his contract,

his site, his men or his materials, he had forgotten the doctor.

One is always hearing of large areas without a doctor. I have traveled through some of those large areas, and there appeared to be little worth while in them, except the train I was riding in. Whole counties in Kentucky do not have a doctor. I used to be dismayed by this until I learned how many counties there are in Kentucky. I have forgotten the number, but it is well up in three figures. What kind of doctor do people want in the mountains of Kentucky and Tennessee? Certainly not a "damn Yankee" doctor. He would not get a chance to practice. A native doctor could practice, but he could not be paid because there is nothing to pay him with. Incidentally, there is no provision in the Wagner-Murray-Dingell Bill that includes these people; it provides only for industrial people, for whom it is compulsory.

As one goes through Massachusetts one finds small settlements, often a so-called "village," without any doctor. One looks at the deserted mills, the deserted farms. One hears someone say, "Most of the people have left, but you'd think some doctor would come." Are doctors people?

Years ago I was on a committee that attempted to study the distribution of doctors, especially in rural communities. We tried to collect cases of hardship, lack of care and forced neglect, but could find only one such case. The complainant was a farmer who testified that on such and such a day he tried to get a doctor to come to see his wife but the doctor would not come. It was in the winter and in the night. His wife had been sick for a couple of weeks but was in "great pain." Somehow or other she got over her illness, but it was terrible, and we were told "Doctors ought not to be allowed to get away with things like that." So we got hold of Doctor Blank. He knew this farmer and occasionally treated him or some member of his family. He had a general idea of where the farmer lived. He was at first rather puzzled by the tale, but finally said:

I'm sure this is the story, but you had better check it with the farmer. It was midwinter and snow was falling. I had just gotten in from a confinement case. After a telephone argument over how sick the wife was, I finally said I'd come, that I would follow the plow the next trip to such and such a corner where the farmer would meet me with a horse and sleigh. That was a common arrangement. However, the farmer said, "Go out on a night like this? I would not send a dog out." Whereupon I hung up.

Subsequently, the farmer verified the complete story, adding that he was tired. To the remark that the doctor might be tired too, he merely replied, "Oh, they get used to it, and if they can't, they ought to do something else."

Now, the Christian Scientist decidedly poohpoohs some of the material things in life, but the "reader" is sound and safe in situations like the

foregoing, because he or she gives the patient absent treatment and does not have to go out in the blizzard of a winter's night.

Just now the armed forces want doctors, physically active ones, for our boys, and the war industries want industrial doctors, while the good folks at home get along courageously with self-rationed medical advice and treatment.

There seems to me to be much too much talk that a doctor is demanded here or there, on this mountain or at this village corner. If doctors were turned out on assembly lines in mass production, it might make sense to talk of so many here and so many there. Of course, the product would be mechanized. What is wanted are good doctors, skilled doctors, not by any means always specialists, but "regular-guy" doctors.

Doctors are human beings notwithstanding the fact they are not supposed to be tired, to have vacations or to enjoy uninterrupted dinners or golf games. For months, on the front pages of most daily newspapers, appeared statements of how soon the draft would begin to take fathers. Senators and representatives in Congress announced that they would fight — in Washington, D. C., not in uniform — to the last ditch the drafting of fathers. Doctors, being ordinary people, seek to marry beautiful and intelligent girls. Doctors' wives have seen their husbands volunteer, even before Pearl Harbor, and leave their homes and children. Many of them have been over thirty-eight and even over forty-five. But doctors were not supposed to object. Since the good women are also human, they sometimes object, but the doctor goes. When the war is over, he will not come back to that salary and that pension, but will be obliged to build up his practice all over again in a world that believes that it created doctors in a certain pattern and therefore can destroy them.

After the war, history will tell of great medical discoveries in it. Plasma and penicillin will be cited. There cannot be found better illustrations of lay domination of medicine. To all intents and purposes, plasma and the theory of plasma was "frozen" — to use the modern jargon — from the end of World War I to the beginning of World War II. Twenty years after World War I, medical scientists continued working as if those twenty years had not existed. The story of penicillin is more picturesque. In 1928, Professor Alexander Fleming, of London, made the observation that germs would not grow with or close to the colony of a common mold. Doubtless other men had observed the same thing, but Fleming puzzled over it and finally published this observation. Years went by and nothing happened. Fleming once showed this phenomenon to me, as he did to many others. Certainly something ought to have been done about it. It was only the threat of war and war itself that furnished the impetus that has produced penicillin. You would

not believe, if I told you, the number of millions of dollars poured into the development of penicillin. It is a new agent in combating infections. It may be that we shall be disappointed in the final place of penicillin, but its present promise dazzles the imagination. And yet without the war no man can ever know whether penicillin would have been developed or how many years it would have taken to develop it. Once again, I must point out to you that the doctors are not the masters of medicine or medical practice, even today.

Certainly the legislature of Massachusetts years ago inflicted a terrible medical practice act on this state, and for years the sovereign Commonwealth of Massachusetts has been the dumping ground for incompetent doctors who were not allowed to take or could not pass the examinations in any other state. Finally the stench reached the Legislature, which recently framed a good bill. But it took a courageous minority of the Board of Registration in Medicine, including fine Dr. Atwood, of Worcester, and a courageous governor to complete the cleansing process of the Augean stables. But what of the hundreds of incompetents who *bought* their licenses to practice medicine in Massachusetts? Thus, it is not the good doctors who determine the standards of medical practice but the community itself. It perhaps creates the doctor in its own image, which can be evil.

It has been to the everlasting credit of the medical profession of this country that traditionally doctors do not patent their discoveries. Recently there has been some wabbling in this attitude. Curiously enough, some medical schools have sought to profit — and some of them have done so mightily — by taking over the patents and the royalties therefrom. The story is told of the opening of the new Harvard Medical School about 1905. A famous New York banker had been a very generous benefactor, but universities are always venal and grasping. The university's star beggar took the New York banker around. The beauties of the buildings were appropriately described. The young scientists were likewise duly noted. "Alas!" said the beggar, "If only we had a little more money to put these trained young men to work." "Humph!" said the banker, "If you have the space and the bright young men, why don't you have one of them invent a good patent medicine? That gives bigger returns than anything I know."

I should like to talk at great length on medical patents and their iniquities, but God be praised, an important court has held a patent that benefited one medical school as invalid, and President Robert Hutchins, of the University of Chicago, has come into the fold of patent purity in medicine. When I am finally sure that any scientist can work with scarlet fever, its germs, its toxins, its antitoxins and its antisera without a special license from the University of Chicago committee on

whatever they call it, I shall write President Hutchins a nice letter congratulating him on seeing the light. But, mind you, this only illustrates the possibilities of lay domination of medical science in accordance, no doubt, with the best Christian practices in business, but leaving the medical men merely puppets.

Now, God forbid that doctors should organize a union, even if that action exempted them from the operation of the anti-trust laws. We do not want any Little Steel Formula. There is too strong a possibility that the other fellow might have a different spelling of "steel."

As I have tried to point out, the lay domination of medicine has been going on since the beginning of time. The medical profession has at times approached independence but it has never been free, certainly not in the way that the profession of law has been independent and free, and master of itself.

Over the years since the turn of the century, there has developed a trend, not new, but for the first time really powerful, that represents a new social philosophy. It came into full flower when social sciences were reorganized as a separate sector of human experience and human knowledge. The enthusiasts of this school of thought lump more or less all the human miseries together. Whereas the doctor looks at his patient through a microscope, the social scientists look at illness through a telescope. Perhaps Sir William Beveridge can be regarded as one of the most articulate, most logical and most reasonable of the exponents of this new social philosophy. He has five giants that must be overcome on the way to "reconstruction," as he calls it — "millennium" is my humble contribution in words. These giants are Disease, Idleness, Ignorance, Poverty and Want. There are other thinkers, perhaps on the outskirts of this philosophic trend, who would mention Superstition, Prejudice, Selfishness and Greed. Within the fold of this cult, however, poverty is the mother of disease. The paternity of disease is usually left obscure. These social scientists would therefore take over disease — the study of disease, the prevention of disease and the treatment of disease — and make themselves masters of medicine and the medical profession. Now, lest you think I am entirely mad, I hasten to add that this, I find, is a favorite theme of a Jesuit priest, Father Schwitalla, who happens to be dean of the St. Louis University School of Medicine, and president of the Catholic Hospital Association of the United States and Canada.

Some years ago I found Professor George Foot Moore, perhaps then Harvard's greatest scholar, in something that in anyone else than a professor and an ordained minister would be called a rage. He had been examining students for the degree of doctor of philosophy. A colleague gave the student a somewhat lengthy case history, which Professor

Moore said was the story of a bum, a very ordinary man. The student candidate was asked for his social diagnosis. When the student answered, "Frustrated childhood in an environment of poverty," Professor Moore exploded. Doubtless there are frustrations, doubtless there is poverty. But I agree with Professor Moore that there are also probably bums, and with Prime Minister Winston Churchill that there are also pub crawlers.

In any event, the social scientist would put disease and the medical profession within the Social Security Act, with a social scientist in the Cabinet. As is evidenced by the Wagner-Murray-Dingell bill, the problem is regarded as economic. Curiously enough, what they want to toss at this hungry, poverty-stricken and diseased wretch is medical service. Now, most doctors would like, so far as possible, to separate the economic and medical aspects. So far as I know, no substantial group of doctors is opposed to the control and relief of poverty, unemployment and the distress of old age, and in the control and relief of poverty doctors would include shelter, warmth, food and the like. And certainly doctors want to have not a better but the best distribution of medical care or "medical service" if you like the new jargon. To the doctor human beings are living entities, not case numbers on a blueprint. Likewise a doctor is a human entity. He is no blue-headed pin to be stuck in a map to take care of so many red-headed pins representing patients.

We all know that in some respects mechanized medicine will work fairly well. You can take the urine of a woman down to the laboratory, and some little laboratory animal will whisper to you whether the woman is pregnant or not. But, for heaven's sake, be careful not to get the bottles mixed. And the impersonal laboratory said authoritatively that Charlie Chaplin was not the father of a certain child. But the mechanization of medicine can be carried too far, and it will be if this present trend continues.

Doctors seem always to have been dominated by others and never to have been complete masters of themselves and of their profession. It seems that this present trend of social, economic and political philosophy threatens them with more dominance than they have ever known. Although I believe this to be a menace to the grandest profession in the world, who am I to venture upon prophecy?

Please note the humility and the altruism of the doctors of Worcester who founded this society one hundred and fifty years ago. This was, a collection of men who planned not to aggrandize themselves but rather to improve themselves, and thereby to benefit the whole community.

Of the same temper are the words in the charter of the Massachusetts Medical Society and that of the American Medical Association. As a class, the doctors have not wanted to run the rest of the world. The late President Lowell, of Harvard, said with regret that the doctor was too busy and too occupied by keeping abreast of the extraordinary medical advances to participate as he should in public affairs, and that the public was greatly the loser thereby. Nevertheless, the public has always wanted its doctors "straight," if you understand that drinking term. The public looked down its nose, and still does, at literary doctors or artistic doctors. And the doctor has shown that he is human and like other folks when he indulges in literature, art or music, usually almost secretly.

But this is not a clarion call for the doctor to dominate the world. Anyway, he knows people too well and himself too well. In his more robust and more individualistic moments, the doctor would like to be more master of his fate and his destiny. But no pedestal for him. In these days of so many words written and spoken about freedom and security, he would like a bit of that freedom in his work. And as for security, his experience makes him skeptical. He has seen diseases vanish and new diseases appear. He has seen trusted remedies become obsolete; he has seen the strong die and the weak get well; he has seen the rich become poor and the poor become rich. He knows that the world is a better and more healthful place in which to live than it was, despite wars, taxes and a large collection of pet hates and aversions of his own.

And so let us turn to a pleasant scene of two elderly doctors, fishing and talking. The fishing was not very brisk, but the talk was brisk and at times salty. Both doctors agreed that the world was in a hell of a mess and what had not already gone to hell was on its way there. Finally one doctor said to the other, "And I suppose if you had your life to live over again, and even knowing what you do, you would be just damn fool enough to be a doctor, the same kind of a doctor, and live the same life." The other doctor answered, "Yep, I suppose so, but I think I'd do more fishing."

CARDIOSPASM AS A CAUSE OF PNEUMONITIS*

WILLIAM GRAY, M.D.,† AND I. R. JANKELSON, M.D.‡

BOSTON

CARDIOSPASM results in dilatation and elongation of the esophagus and a secondary esophagitis caused by a variable degree of food retention. Whenever ingesta are retained in the esophagus, — and in cardiospasm the capacity of the esophagus may be a quart or more, — there is danger of inhalation of food, saliva or secretions, which may lead to the development of an inhalation pneumonia, lung abscess, chronic bronchitis or bronchiectasis.

Jackson and Jackson¹ have rightly emphasized that such inspiration is especially likely to occur with obstruction in the upper portion of the esophagus, particularly in the presence of a carcinoma. They describe nine means by which pulmonary symptoms can be developed by pathologic conditions in the esophagus. Of these only one applies to cardiospasm. The pulmonary involvement secondary to a pre-existing cardiospasm is due to regurgitation of food or secretions, which is particularly prone to occur during sleep when the normal protective reflexes are less sensitive. Thus food particles from the large reservoir in the esophagus may be inhaled. Sudden awakening with coughing, choking and strangling is not infrequent in cases of esophageal food retention. Moreover, Rastelli² and Camiel and Loewe³ demonstrated by roentgenoscopic and roentgenographic methods frequent spilling of barium into the trachea and bronchi in obstructive lesions of the esophagus. This demonstrates that inspiration of food and secretions may occur during waking hours as well as in sleep. It is likelier to occur in debilitated, emaciated and dehydrated persons, whose reflexes, like all other body functions, are less active than those of others. Minimal inspiration leads to some strangling and coughing, and massive inhalation may lead to serious pulmonary disease.

Two such cases that recently came to our attention are reported below.

CASE REPORTS

CASE 1. C. T. (B. I. H. 71845), a 45-year-old, married woman, was admitted to the Beth Israel Hospital with a 4-year history of dysphagia and a 3-year history of vomiting and regurgitation. The vomiting occurred several times daily, the vomitus consisting of mixtures of partially digested and unchanged food. The patient frequently awoke from sleep to find her mouth full of regurgitated food, some of which had run out on the pillow. Attacks of sharp pain located in the midback region on the right side had begun 2 years previously, and as time went on this pain became more

diffuse and was transmitted to the right side of the neck. Four months prior to entry into this hospital, the patient developed a cough productive of large amounts of mucopurulent material, associated with pain in the bilateral posterior part of the chest and fever. Because of these symptoms she entered another hospital. During the next 2 months she had three attacks of fever, cough and chest pain, each episode lasting about 10 days. X-ray films of the chest taken at that hospital showed bilateral bronchopneumonic changes and although sputum and gastric washings were negative for acid-fast organisms, a diagnosis of pulmonary tuberculosis was made and the patient was transferred to a tuberculosis sanatorium for further care. During her 2-month stay there, almost continuous vomiting and regurgitation with progressive emaciation took place, and a fourth attack of high fever associated with cough, diffuse rales and patchy dullness in both lung fields occurred. This attack lasted for 9 days.



FIGURE 1. Roentgenogram of Esophagus (August 4, 1943). Fluoroscopic and roentgenographic examinations showed the esophagus to be markedly widened and tortuous. In this film the upper two thirds of the esophagus is mottled, owing to retention of food and secretions. These findings are typical of cardiospasm.

and did not respond to chemotherapy. Repeated sputum examinations were negative for tubercle bacilli.

Because of doubt concerning the accuracy of the diagnosis of pulmonary tuberculosis, the patient was transferred to this hospital for further study and treatment. At the time of entry she presented a picture of extreme emaciation, weigh-

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only 85 pounds, whereas 4 years previously she had weighed 140 pounds.

Physical examination revealed an apprehensive woman with a rectal temperature of 102° F., a pulse of 110 and a respiratory rate of 32. The pharynx was diffusely reddened and showed considerable lymphoid hyperplasia. Examination of the lungs showed dullness to percussion over both sides, with crepitant rales over the lower part of both lungs, more marked on the right side than on the left. Heart sounds were hyperactive, and there was a harsh, systolic murmur heard best just to the left of the

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On the 46th day, the temperature again rose to 104° F. and signs of extensive bronchopneumonia reappeared in both lung fields. Sulfadiazine was again started, but it was given by mouth, as were food, fluids and other medications. The diet consisted of fluids and semisolid foods only. The patient continued to run a spiking temperature with daily variations between 101 and 104° F. until the 59th day, when sulfadiazine was omitted. The temperature continued to be elevated until the 64th day, when it returned to normal, in association with clearing of the signs of pneumonia.

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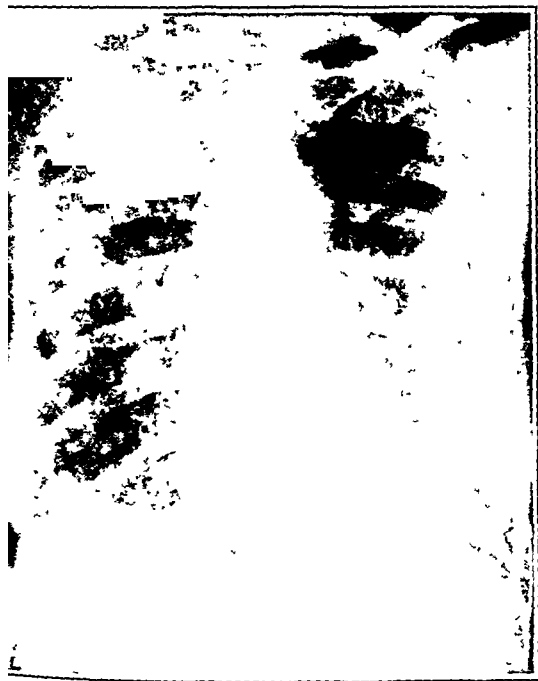


FIGURE 2. Roentgenogram of Chest (August 4).

This film shows mottled density involving the lower two thirds of both lungs, more marked on the right, that is consistent with bronchopneumonia.

num in the 3rd intercostal space, but the heart size was within normal limits. Moderately severe clubbing of the fingers and minimal clubbing of the toes were present.

X-ray examination of the chest on admission showed findings consistent with bronchopneumonic consolidation in the right upper lobe and resolving patchy pneumonic consolidation throughout both lung fields. At the time this film was taken, it was noted that the heart appeared to be slightly rotated to the right. Because of this, the patient was sent to the X-ray Department on the following day for fluoroscopy of the heart. At that time a horizontal fluid level was seen in the upper posterior mediastinum. The patient was then given a swallow of barium and it was found that the esophagus was markedly dilated and tortuous (Figs 1 and 2). In report of this examination stated, "The convex contour previously interpreted as a dilated right heart, turns out to be the contour of the tortuous, dilated esophagus typical of cardiospasm." Only small amounts of barium were seen trickle through the cardia into the stomach. The stomach and duodenum were normal. Another x-ray film of the chest taken on the 10th hospital day showed no essential change from the previous examination. On that day the temperature rose to 104° F., with an elevation of the respirations to 50 and of the white-cell count to 20,000. Associated with this there appeared increasing signs of bronchopneumonic consolidation throughout both lungs. From the 10th to the 13th day, the temperature ranged between 101.0 and 105.5° F. X-ray examination of the chest on the 13th day showed markedly increased consolidation throughout the lower two thirds of both lung fields (Fig. 3). On the 16th day, it was finally decided that the patient had aspiration pneumonia

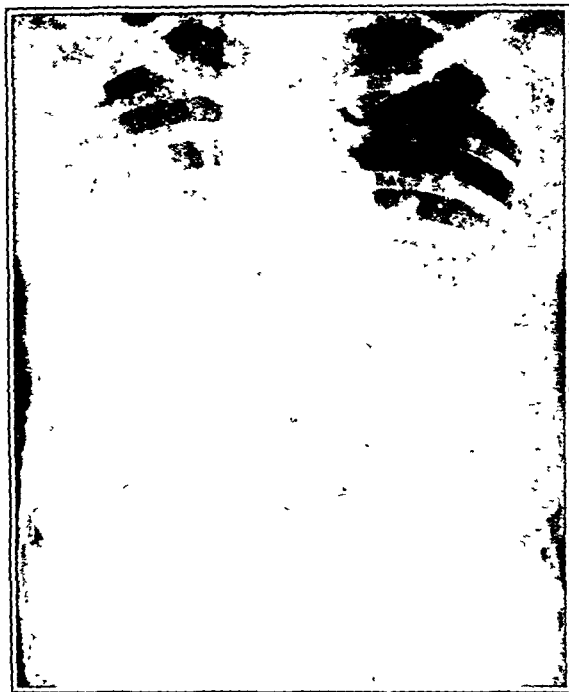


FIGURE 3. Roentgenogram of Chest (August 17).

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esophagus, the cardiospasm and the lack of normal sensation in the esophagus and bronchial tree accounted for the spilling of food from the dilated esophagus into the respiratory tract.

X-ray examination of the chest on the 73rd day showed partial clearing of the pulmonary infiltration (Fig. 4). Fluoroscopic examination of the esophagus on the 83rd day still showed a dilated, atonic esophagus, but there was great improvement in the ease with which barium flowed from the esophagus into the stomach.

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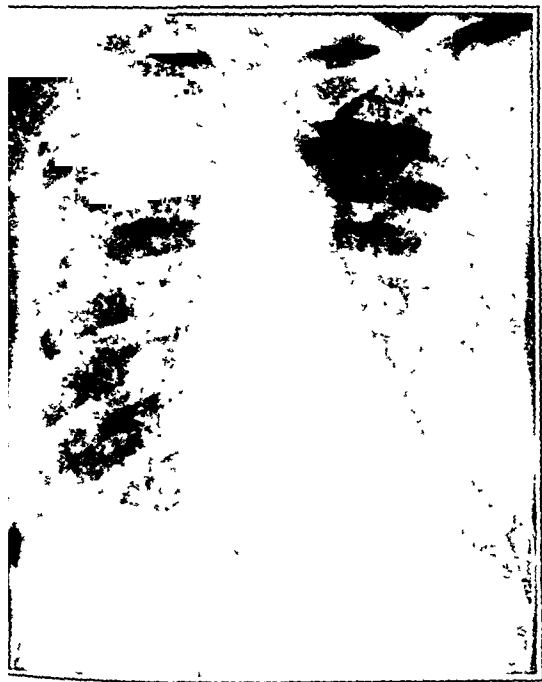


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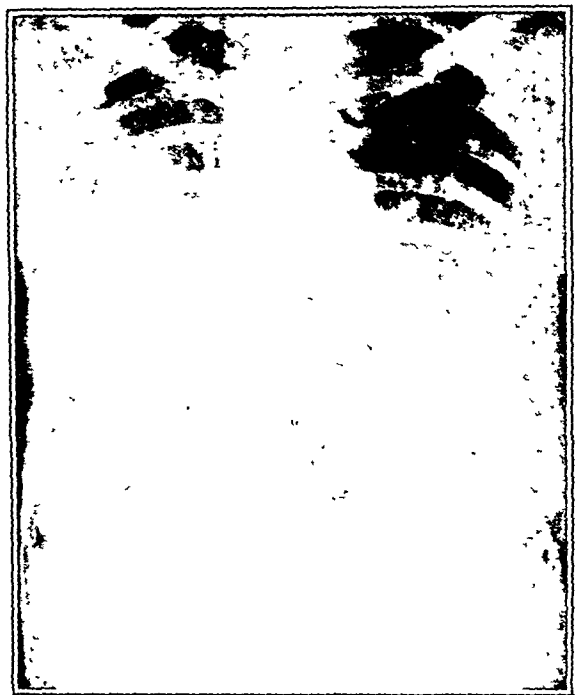


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The temperature remained normal from the 64th to the 86th day, when the patient was discharged. She stated that she felt much improved and that she was able to swallow more easily than she had for years. Furthermore, regurgitation of food was almost completely absent. During the hospital stay the patient gained 10 pounds in spite of the two prolonged attacks of aspiration pneumonia.

Four days after discharge, the patient again began to regurgitate and developed a temperature of 101.4° F., as a result of which she was readmitted. On examination only a few rales could be heard at the lung bases. The temperature returned to normal on the 2nd hospital day with the use of symptomatic therapy only. The patient was kept in the

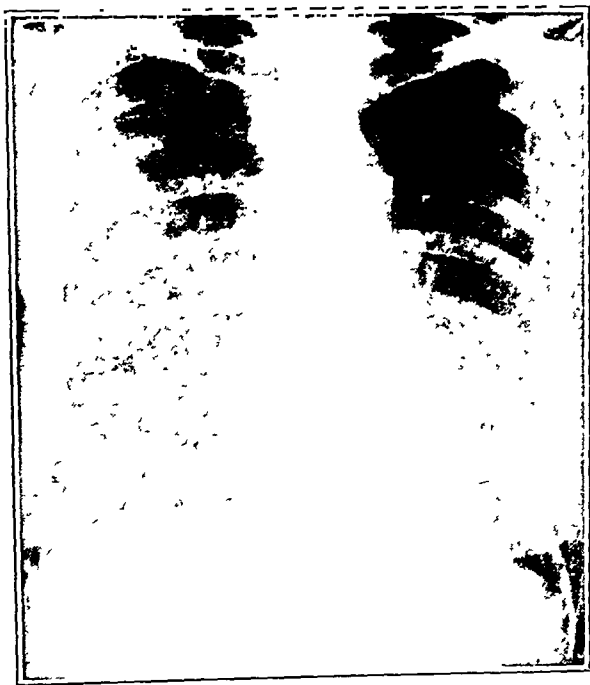


FIGURE 4. Roentgenogram of Chest (January 19, 1944). This film shows considerable clearing in both lungs, consistent with resolving pneumonia.

hospital for 2 weeks, and throughout this period manifested no more signs of pneumonia and no further fever; regurgitation did not recur.

Three months after the second discharge, the patient was again seen in the Outpatient Department. She was still well and her weight had increased to 108 pounds, a gain of 23 pounds from the lowest weight 4 months previously. Some regurgitation was still present, but swallowing was much easier than it had been in the preceding 4 years. The patient reported that she had no trouble at all in swallowing liquid and semi-solid foods. X-ray examination of the chest still showed some scattered infiltration throughout both lung fields, which was interpreted as due to pulmonary fibrosis. Fluoroscopic and radiographic examination of the esophagus revealed continued improvement, but some retention was still present. During these 3 months, the patient had been completely free of fever and her cough had decreased markedly. Another esophageal bouginage was done.

CASE 2. M. E., a 34-year-old woman, had had a history of dysphagia for 10 years. The amount of discomfort varied from time to time, but she was never completely free of symptoms. The difficulty in swallowing was more marked when she partook of solid food. Liquid and mushy food was swallowed with little or no distress. Throughout these years there was considerable gagging and choking. There were also frequent coughing spells and occasional bringing up of food particles. The patient had lost 18 to 20 pounds in weight and felt weak and tired. During these 10 years the patient had four attacks of pneumonia, the first episode occurring 8 years previously. Six years previously, she had a diffuse bronchopneumonia, at which time her life was despaired of,

and ran a febrile course for at least 6 weeks; careful bacteriologic studies revealed no pneumococci in the sputum or the blood. Another attack of pneumonia, relatively mild in character, occurred 4 years previously. The last attack occurred 2 years previously, when the patient was again seriously ill for 5 weeks. Following the pneumonia 6 years previously, she developed a polyneuritis that was ascribed to vitamin deficiency, apparently precipitated by the prolonged fever and inability to partake of adequate food. She recovered after vigorous parenteral administration of various preparations of vitamin B. The patient presented herself for the treatment of the dysphagia, which in recent months had become aggravated and was accompanied by frequent regurgitation of undigested food.

Physical examination was essentially negative except for evidence of weight loss and moderate dehydration. Roentgenoscopic and roentgenologic examination revealed a markedly dilated and tortuous esophagus with a typical funnel-shaped subdiaphragmatic portion. No barium was seen to pass into the stomach during this examination. The following day the esophagus was dilated under fluoroscopic control and was found still to contain barium. Following this manipulation, barium was seen to enter the stomach. A complete gastrointestinal roentgen-ray examination 2 days later revealed no other disease within this tract. Roentgen-ray examination of the chest was negative.

Within the next 5 weeks, the patient had further dilatations of the esophagus at weekly intervals. The dysphagia improved markedly. She gained 12 pounds in weight and the gagging and choking while taking food, as well as between meals, disappeared.

DISCUSSION

These cases demonstrate two types of pneumonic involvement secondary to a cardiospasm. The first case represents a chronic pneumonitis with repeated exacerbations, presumably due to repeated insults to the affected lung tissue. In this case the significance of the esophageal symptoms in the evaluation of the illness was overlooked for a period of four months because of the predominance of the pulmonary symptomatology. The second case is characterized by repeated acute pneumonic processes, with long periods of intervening relatively good health. A review of recent current literature reveals only a few similar cases. Hoover⁴ reported a case in which a patient with a chronic pneumonitis, apparently of five years' duration, was cured by esophageal dilatations. Tucker⁵ reported a case of chronic pneumonitis in a thirteen-year-old boy who had cardiospasm. Thomas and Jewett⁶ reported the case of a thirty-two-year-old man who had a greatly dilated esophagus due to cardiospasm and died of bilateral pneumonia. He had been receiving feedings of cream as part of a high-caloric diet. At autopsy, histologic examination showed the pneumonia to be of the type produced experimentally in animals by instilling oil into the lungs. Reports of lung-abscess formation, the result of inspiration of retained food in the esophagus, are more numerous, but neither this condition nor suppurative peribronchitis is discussed here.

The establishment of a causal relation may be difficult in a single case. In fact, it is undoubtedly frequently overlooked or a correct diagnosis is made only in retrospect. Jackson and Jackson¹ consider the demonstration of food residue in the pyriform sinuses an indication of esophageal stenosis in which

verflow into the larynx is a possibility. This sign should be looked for in every case of etiologically obscure pneumonitis. The demonstration of inspiration of barium into the tracheobronchial tree is convincing evidence of a causal relation. The observation that the patient coughs up food particles or, as in one of these cases, ingested tablets, should suggest the possibility of an inspiration pneumonia. Finally, a bronchoscopic examination may elicit important diagnostic evidence.

Since the right bronchus is nearer to the vertical than is the left, foreign bodies enter it more frequently than they do the left bronchus, so that most inhalation pneumonias primarily involve the right lung, but a bilateral involvement occurs in cases of massive inspiration. In such cases rapid exitus is the rule.

Repeated dilatations of the esophagus, which minimize the food retention, are recommended in the prophylaxis of inhalation pneumonia as well as in the treatment of this condition. Between attacks of pneumonia, transthoracic plastic surgery of the esophagus should be considered.

SUMMARY

Two cases of cardiospasm complicated by inhalation pneumonitis are reported. This pneumonitis may be either of the recurrent acute type or of the chronic type with acute exacerbations. The alleviation of the cardiospasm by bouginage improves the general condition and contributes to the cure of the pneumonic process. It is recommended that the esophagus be investigated routinely in all cases of etiologically obscure chronic pneumonitis or recurrent acute pneumonia.

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Corrections. In the article "Paget's Disease: Its pathologic physiology and the importance of this in the complications arising from fracture and immobilization" by Drs. E. C. Reifstein, Jr., and Fuller Albright, which appeared in the September 7 issue of the *Journal*, two corrections should be made. In the ninth line of the sublegend of Figure 1, the word "hyperplasia" should be "hypoplasia." In the twenty-seventh line of the first column on page 351, the figures "135/195" should be "135/95."

The temperature remained normal from the 64th to the 86th day, when the patient was discharged. She stated that she felt much improved and that she was able to swallow more easily than she had for years. Furthermore, regurgitation of food was almost completely absent. During the hospital stay the patient gained 10 pounds in spite of the two prolonged attacks of aspiration pneumonitis.

Four days after discharge, the patient again began to regurgitate and developed a temperature of 101.4° F., as a result of which she was readmitted. On examination only a few rales could be heard at the lung bases. The temperature returned to normal on the 2nd hospital day with the use of symptomatic therapy only. The patient was kept in the



FIGURE 4. Roentgenogram of Chest (January 19, 1944). This film shows considerable clearing in both lungs, consistent with resolving pneumonia.

hospital for 2 weeks, and throughout this period manifested no more signs of pneumonia and no further fever; regurgitation did not recur.

Three months after the second discharge, the patient was again seen in the Outpatient Department. She was still well and her weight had increased to 108 pounds, a gain of 23 pounds from the lowest weight 4 months previously. Some regurgitation was still present, but swallowing was much easier than it had been in the preceding 4 years. The patient reported that she had no trouble at all in swallowing liquid and semi-solid foods. X-ray examination of the chest still showed some scattered infiltration throughout both lung fields, which was interpreted as due to pulmonary fibrosis. Fluoroscopic and radiographic examination of the esophagus revealed continued improvement, but some retention was still present. During these 3 months, the patient had been completely free of fever and her cough had decreased markedly. Another esophageal bouginage was done.

CASE 2. M. E., a 34-year-old woman, had had a history of dysphagia for 10 years. The amount of discomfort varied from time to time, but she was never completely free of symptoms. The difficulty in swallowing was more marked when she partook of solid food. Liquid and mushy food was swallowed with little or no distress. Throughout these years there was considerable gagging and choking. There were also frequent coughing spells and occasional bringing up of food particles. The patient had lost 18 to 20 pounds in weight and felt weak and tired. During these 10 years the patient had four attacks of pneumonia, the first episode occurring 8 years previously. Six years previously, she had a diffuse bronchopneumonia, at which time her life was despaired of,

and ran a febrile course for at least 6 weeks; careful bacteriologic studies revealed no pneumococci in the sputum or the blood. Another attack of pneumonia, relatively mild in character, occurred 4 years previously. The last attack occurred 2 years previously, when the patient was again seriously ill for 5 weeks. Following the pneumonia 6 years previously, she developed a polyneuritis that was ascribed to vitamin deficiency, apparently precipitated by the prolonged fever and inability to partake of adequate food. She recovered after vigorous parenteral administration of various preparations of vitamin B. The patient presented herself for the treatment of the dysphagia, which in recent months had become aggravated and was accompanied by frequent regurgitation of undigested food.

Physical examination was essentially negative except for evidence of weight loss and moderate dehydration. Roentgenoscopic and roentgenologic examination revealed a markedly dilated and tortuous esophagus with a typical funnel-shaped subdiaphragmatic portion. No barium was seen to pass into the stomach during this examination. The following day the esophagus was dilated under fluoroscopic control and was found still to contain barium. Following this manipulation, barium was seen to enter the stomach. A complete gastrointestinal roentgen-ray examination 2 days later revealed no other disease within this tract. Roentgen ray examination of the chest was negative.

Within the next 5 weeks, the patient had further dilatations of the esophagus at weekly intervals. The dysphagia improved markedly. She gained 12 pounds in weight and the gagging and choking while taking food, as well as between meals, disappeared.

DISCUSSION

These cases demonstrate two types of pneumonic involvement secondary to a cardiospasm. The first case represents a chronic pneumonitis with repeated exacerbations, presumably due to repeated insults to the affected lung tissue. In this case the significance of the esophageal symptoms in the evaluation of the illness was overlooked for a period of four months because of the predominance of the pulmonary symptomatology. The second case is characterized by repeated acute pneumonic processes, with long periods of intervening relatively good health. A review of recent current literature reveals only a few similar cases. Hoover⁴ reported a case in which a patient with a chronic pneumonitis, apparently of five years' duration, was cured by esophageal dilatations. Tucker⁵ reported a case of chronic pneumonitis in a thirteen-year-old boy who had cardiospasm. Thomas and Jewett⁶ reported the case of a thirty-two-year-old man who had a greatly dilated esophagus due to cardiospasm and died of bilateral pneumonia. He had been receiving feedings of cream as part of a high-caloric diet. At autopsy, histologic examination showed the pneumonia to be of the type produced experimentally in animals by instilling oil into the lungs. Reports of lung-abscess formation, the result of inspiration of retained food in the esophagus, are more numerous, but neither this condition nor suppurative peribronchitis is discussed here.

The establishment of a causal relation may be difficult in a single case. In fact, it is undoubtedly frequently overlooked or a correct diagnosis is made only in retrospect. Jackson and Jackson¹ consider the demonstration of food residue in the pyriform sinuses an indication of esophageal stenosis in which

chloride, associated with an increase in sodium and bicarbonate. The serum pH was 7.6, and the authors referred to the condition as "an asymptomatic alkalosis of a severe grade." This association of alkalosis and low serum potassium was observed also by Willson, Power and Kepler,⁶³ but in this case tetany was present. Talbot, Butler and MacLachlan⁶⁴ administered methyl testosterone and testosterone propionate to an eight-year-old girl suffering from Addison's disease in an attempt to restore muscular strength, and recorded a striking reduction in serum potassium to 1.9 milliequiv. per liter. They state:

The marked lowering in the serum potassium concentration while the patient was receiving testosterone was not associated with clinical evidence of muscular weakness or paralysis. On the contrary, the patient seemed to benefit from the testosterone, as evidenced by gain in weight, growth in stature and apparent increase in strength and endurance.

They suggest that one of the mechanisms operating in the gain in weight was an increase in intracellular water.

From these observations, and from the experimental evidence that indicates an influence of adrenocortical and associated hormones on the level of serum potassium, Darrow⁶⁵ concludes that deficit of potassium occurs in other clinical conditions, and that unexplained high bicarbonate, low chloride and low potassium in the serum may be the findings that will lead to the discovery of cases. Two subsequent reports bear out his predictions. In a case of Addison's disease in which death occurred in heart failure, histologic changes were seen similar to those found in potassium deficiency.⁶⁶ It was thought that the heart failure resulted from a low serum potassium level, produced by a combination of desoxycorticosterone pellet therapy and a low potassium intake due largely to failure to eat. No potassium determinations were made, however, during the premortal hospitalization, and values during a previous hospital admission were normal. A bibliography of the subject of low potassium is found in this paper and in Darrow's review. Low potassium with an entirely different etiology is reported by Brown, Currens and Marchand.⁶⁷ In their 2 cases there appeared to be an excessive loss of potassium due to renal insufficiency in chronic nephritis, and the serum potassium fell to 2 milliequiv. per liter. The patients complained of extreme muscular weakness, fatigue and paralysis, the T waves in the electrocardiogram were of low voltage and the oral administration of potassium salts appeared to be of benefit.

CURARE

No drug has attracted interest among physiologists equal to that curare has aroused nor proved so useful as a technical tool or as a stimulus to new investigations. Few drugs have had less clinical usefulness. Physiologists are therefore likely to

watch with interest the application of this drug to a variety of purposes for which its unique physiologic properties may prove useful. The most recent and potentially the greatest use is in anesthesia, to secure or to enhance relaxation of skeletal muscle during surgical operations. It was given its first clinical trial in Montreal by Griffith,^{68,69} who has employed it with considerable reservation in situations in which it is impossible or too hazardous to obtain relaxation with the anesthetic agent alone. Cullen⁷⁰ employs the drug more freely, to obtain relaxation rather than to increase the concentration of the anesthetic agent. His practice is to carry the patient in light second-plane inhalation anesthesia and, with proper doses of curare, to obtain relaxation. This is achieved by intravenous injection of at least 0.06 gm. (3 cc.) of the commercial extract (Intocostrin-Squibb), although usually 0.1 gm. is required in the average patient under cyclopropane anesthesia. Ether apparently interferes directly with neuromuscular transmission⁷¹ and requires that the dose of curare be reduced to one third of that used during cyclopropane anesthesia. There is a report that curare has a direct depressant action on the respiratory center,⁷² but the diminution in frequency and depth of respiration noted in an early stage of curarization may represent the reaction of the center to the diminution in reflex drive that must occur as skeletal muscles begin to be paralyzed and fail to set up the reflex stimulus to respiration for which they are normally responsible.⁷³

Curare has also been employed to cushion the convulsions in therapeutic shock,⁷⁴ to prevent the convulsions in tetanus⁷⁵⁻⁷⁷ and as a temporary relief in spastic states.⁷⁸ When employing the drug in these situations, as well as in anesthesia, it is necessary to remember always that the muscles of the respiratory center become paralyzed at very nearly the same level of dosage as do other skeletal muscles, and that it may therefore be necessary to employ artificial respiration. Since with the complete loss of muscle tone caused by the drug the chest has little natural elasticity, chest-pressure methods are ineffective, and those employing positive air pressures must be employed.

DETECTION OF TIME OF OVULATION

Burr, Hill and Allen⁷⁹ noted that an increase occurred in the potential difference between a vaginal and a suprapubic electrode at the time of ovulation in the rabbit, and these findings have been confirmed in other species.⁸⁰⁻⁸⁶ The same phenomenon was shown to occur in women,⁸⁷⁻⁹⁰ and has been advocated as a means of determining the time of ovulation. The cause of the phenomenon has supposedly been electrical potentials developing between the ovary and other organs owing to rupture of the follicle. Study of such potentials in women on whom laparotomies were performed indicated that the potential changes might develop before

MEDICAL PROGRESS

PHYSIOLOGY (Concluded)*

HEBBEL E. HOFF, M.D.†

MONTREAL, CANADA

POTASSIUM POISONING IN MAN

In 1915, Smillie⁴⁷ reported a temporary episode of collapse with vomiting following the administration of 10 gm. of potassium chloride to a patient suffering from chronic nephritis with uremia. He called attention to the greatly increased toxicity of potassium salts when excretion in the urine was prevented by damage or extirpation of the kidneys in experimental animals. On the basis of these observations he suggested that spontaneous auto-intoxication by the potassium salts liberated in cell metabolism might occur in man if renal elimination of potassium were interrupted. This hypothesis became susceptible of proof through the work of Winkler and his co-workers,⁴⁸ who demonstrated a characteristic series of electrocardiographic changes occurring when experimental animals were poisoned with potassium administered intravenously, and who also showed that this sequence of electrocardiographic changes took place as successively higher levels of serum potassium were attained. In the absence of renal excretion of potassium, poisoning by means of orally administered potassium became possible,⁴⁹ and animals in which the kidneys were removed or the ureters tied invariably succumbed to autointoxication.⁵⁰

Reports are now at hand indicating that an identical situation may develop in man. The first of these comes by coincidence from the Medical Clinic of the Peter Bent Brigham Hospital,⁵¹ where Smillie's original observations were made. It concerns 2 patients with marked oliguria who were given potassium chloride by mouth as a therapeutic measure. In both patients electrocardiographic changes developed that were in every way similar to those shown by dogs in the course of potassium poisoning, and the level of serum potassium at death, examined in one of the patients, agreed with that found in the dog. The same authors⁵² have now reported 2 cases in which potassium poisoning occurred spontaneously, without the administration of potassium salts. Three additional cases have been presented by Keith, Burchell and Baggenstoss⁵³ in which the accumulation of potassium occurred in uremia due to kidney disease.

In accord with a suggestion in an earlier progress report in this series,⁵⁴ it is now reported that in the anuria associated with the crush syndrome potassium intoxication may be responsible for death. Bywaters⁵⁵ reports as follows:

Two thirds of the patients die toward the end of the first week, the majority on the sixth day. Death occurs very suddenly and may be preceded by cardiac irregularity. If electrocardiographic tracings are taken, changes similar to those seen in human potassium poisoning are seen—increased T waves and widened QRS complexes. These are associated with an increase of the potassium level in the serum to more than twice the normal upper level of 20 mg. per 100 cc. The raised serum potassium concentration in crushing injury is due to two processes: first, the muscle potassium diffuses out into the blood stream, its concentration falling from 300 to 70 mg. per 100 cc. or lower, both in man and in animals; secondly, very little of this is excreted owing to renal failure, and thus it accumulates in the body.

In these descriptions of fatal poisoning in man, the maintenance of blood pressure and consciousness until the onset of cardiac arrest is a striking feature, and suggests the value of electrocardiographic examination of anuric and oliguric patients. Marchand and Finch⁵² mention temporary success in restoring the normal heart beat with calcium salts, and Bywaters⁵⁵ suggests the use of glucose and insulin, based on the observation (Fenn⁵⁶) that potassium may be withdrawn from the circulation and deposited in the liver when glucose is laid down as glycogen.

The possibility of another type of potassium poisoning is suggested by the observation of an extremely high blood potassium value (287 mg. per 100 cc.) found post mortem in a woman succumbing to the effects of a soft-soap paste inserted into the uterus to produce an abortion.⁵⁷ The blood cells were completely hemolyzed, and the supposition is expressed that the potassium normally contained in the red cells was released by the hemolysis and raised the effective serum concentration to a lethal level. It is apparent, also, that although fatal potassium poisoning is not a frequent mode of death in experimental traumatic shock or adrenal insufficiency, it occasionally occurs in both of these conditions when survival is prolonged in the presence of oliguria.⁵⁸⁻⁶⁰

Circumstances in which the serum potassium level is abnormally low will probably prove to be more frequent and of greater clinical significance than those in which it is elevated. Familial periodic paralysis is the first well-recognized example. Occasional reports indicate that Cushing's disease may be another. Walters, Wilder and Kepler⁶¹ reported a case that was successfully treated by subtotal resection of the adrenal glands, in which low pre-operative levels (10.4 and 9.3 mg. per 100 cc.) rose to the upper limits of normal (24.6 and 25.5 mg.) after operation. McQuarrie, Johnson and Ziegler⁶² noted a marked reduction in serum potassium and

*From the Department of Physiology, McGill University.

†Professor of physiology, McGill University.

THE NEURONE THEORY

A review by Nonidez¹¹¹ of the present status of the neurone theory reminds physiologists of the extent which the present structure of neurophysiology is dependent on and associated with the neurone theory. His summary is quoted in full as an admirable account of the recent history of the neurone theory:

During the last decade certain authors have considered the classical neurone theory to be obsolete and have resuscitated the long-rejected hypothesis of a nervous syncytium, mainly on histological evidence. Bauer believes in connexions between embryonic neuroblasts, serving as pathways for the growth of nerve fibers which thus develop intraplastically. This concept must be regarded as entirely hypothetical. Anastomoses found between neuroblasts and nerve fibers growing in tissue culture are emphasized by the reticularists, but this is not overwhelmingly against the neurone theory, since such anastomoses are by no means universal and they depend on the part of the nervous system cultured and on the properties of the medium. Claims by Bauer on the continuity of nerve cells with each other and with neuroglia disagree with the demonstrated existence of free dendrites and of synapses with neurones. Reticularists also maintain the continuity of neurones in the autonomic system, but this too is open to criticism on histological grounds. Moreover, autonomic ganglia afford good material for the demonstration of synaptic endings both in fixed and living preparations. The reality of independent neurones is confirmed by the degeneration of synaptic boutons in the central nervous system after the destruction of nerve tracts, and by the degeneration and regeneration of preganglionic fibers in autonomic ganglia, in which the loss and recovery of function are confirmed experimentally. The existence of the synapses is confirmed by the decay in impulse transmission, varying with the type of synapse, and by the nicotine block to impulses from preganglionic fibers to autonomic ganglia. The recent criticisms of the neurone theory are based on preparations made exclusively by the Bielschowsky technique, unsupported by experimental work, and the several workers disagree widely in their evidence. Boeke claims that the finer divisions of the autonomic system contain a meshwork of neurofibrils clearly distinguishable from the surrounding connective tissue; this structure is not found, however, with other neurofibrillar methods but appears with silver carbonate, which does not stain nervous structures. Stöhr believes in a fine terminal reticulum of the autonomic and sensory systems surrounding every cell in the body. Again other competent histologists, working with techniques which do not stain connective tissue, have failed to confirm Stöhr, whose claims are moreover unsupported experimentally. The reticularists cannot agree among themselves on their substitute for the neurone theory, and it would seem wise to retain this concept until better proof is offered of the syncytial nature of the nervous system.

ORIGIN OF HEART BEAT

The cause of the heart beat presents perhaps the oldest and most controversial problem in physiology; a great part of it is now of historical interest only.^{112, 113} So far as the vertebrate heart is concerned, the long disputes between adherents of the neurogenic and myogenic theories may be said to have resulted in the complete victory of the latter doctrine. However this may be, recent evidence indicates that in acting as pacemaker to the heart the muscular tissue of the sinus venosus or sino-auricular node behaves very much as does a nerve fiber, nerve cell, sense organ or even skeletal muscle in certain circumstances.

With the discovery of the refractory period in the heart,¹¹⁴ it became possible to construct the first rational theory of the origin of the heart beat, as due to the presence of a constant inner stimulus, which set up a beat whenever the heart recovered sufficiently from the refractoriness caused by the previous discharge. This simple explanation appears to account for the repetitive firing of a nerve fiber injured at one end, the local injury current acting as the constant stimulus. In the nerve cell this explanation proved inadequate to account for the relatively slow rhythms exhibited by such neurones as the soleus motoneurone, in which the interval between beats is many times the known absolutely refractory period. With the recognition of the subnormal period, this problem was solved, for it was realized that the motoneurone may show a depression of irritability long outlasting the absolutely refractory period, and that discharge can only occur at the end of this period, when the threshold falls toward normal.¹¹⁵ In the heart even this extension of theory proves inadequate, because it has been repeatedly found that a gradually falling threshold is only occasionally seen, and that usually the threshold remains level for some time before a new beat occurs. This is particularly true of the pacemaker itself, where, in fact, a period of supernormal recovery is at times found.¹¹⁶ This obviously indicates that the inner stimulus of the heart cannot be constant in intensity but is intermittent. This is now established in the vertebrate heart through the work of Bozler,¹¹⁷⁻¹¹⁹ who has studied electric potentials in pacemakers in the smooth muscle of the ureter and small intestine, and in turtle, dog, cat and guinea-pig heart muscle. Apparently pacemaker activity is the result of the spontaneous development of slow rhythmic oscillations of potential, which are found only in pacemaking tissue. These potentials are closely allied to rhythmic oscillations between the negative and positive after-potentials, and if they are sufficiently intense, — about one fiftieth of the normal spike potential, — propagated discharges are set up at their negative crests. These spontaneous, slow, potential changes — so-called "prepotentials" — are apparently the direct cause of the heart beat. They may be increased, or even developed in the heart, by anodal polarization,¹²⁰ and in nerve and skeletal muscle their appearance is facilitated by low calcium and alkalinity.¹²¹⁻¹²³ Although the point has not been settled, it is possible that the so-called "pre-sinus" waves noted by Rijlant¹²⁴ represent prepotentials in the mammalian pacemaker.

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ovulation occurred, leading to an extensive study of the problem, which has been published recently.^{91,92} The most crucial observations in this study consist in the failure to detect any potential differences between any two organs in the abdominal cavity greater than about 1 millivolt in 3 women during the course of routine laparotomies performed during the calculated ovulation time. Several follicular surfaces, including that of one fairly large, presumably mature follicle, as well as the intervening ovarian cortex, were tested, but no significant electrical potential was detected. It being concluded that the potentials measured were therefore restricted to the surface, the influence of temperature differences between recording skin surfaces was investigated, and was found to be of the average of 1 millivolt per degree Centigrade in finger-to-finger potentials. The temperature difference between vagina and various skin reference points was also found to be related to vagina-to-skin potentials. Changes in the pH of the skin were seen to affect the potentials recorded between the skin and the vagina. From these studies the conclusion was drawn that "so-called ovulation potentials previously reported, whether elicited between a vaginal and a suprapubic electrode, between two surface areas — abdominal or flank — or between fingers, are measurements only of local changes in peripheral cutaneous blood flow, owing to alterations in capillary tone." Experimental data and calculations indicate that the potential shifts may be occasioned by pH alterations induced by temperature changes.

Although these experiments render it highly unlikely that the so-called "ovulation potentials" arise directly in the ovary as the result of ovulation, they do not detract from the evidence hitherto adduced that they are indeed closely associated with ovulation in time. They do suggest that the method is possibly only a roundabout method of detecting changes in temperature associated with ovulation. Indeed, there is a recurring interest in the use of basal temperature graphs in determining the data of ovulation.⁹³⁻⁹⁷ Tompkins⁹³ reports as follows:

A record of body temperature taken daily under standard conditions shows a typical curve during the menstrual cycle. The temperature is relatively low during the first part of the month, drops to a minimum about the time that ovulation occurs and rises definitely thereafter to a relatively high level, which is maintained until the next menses, when the temperature drops abruptly. Before the menarche, after the menopause and in men, similar temperature fluctuations are not found. If conception occurs, the temperature will remain at the high postovulation level. The important feature is the rapid rise in temperature at ovulation.

Certain evidence in favor of this method comes from Greulich and Morris,⁹⁸ who recorded morning rectal temperatures daily during successive cycles in 14 women aged fifteen to thirty-nine years. In all of them laparotomies were performed and the ovaries were inspected. Eight women showing a characteris-

tic postovulatory temperature rise preceding the operation were found in fact to have ovulated. Five women showed no rise in temperature before operation and were found not to have ovulated. In 1 case a slight rise in temperature began before operation, and sections from the ovary suggested that ovulation was about to take place. This of course fits in with the observation that ovulation potentials may be seen before ovulation begins.^{89,90} In the belief that the temperature changes taking place during ovulation are more marked in the uterus, Klawns⁹⁹ has devised a thermometer by which uterine temperatures may be taken. The evidence he presents does not appear to indicate any decided advantages for this method.

BRITISH AND AMERICAN HEMOGLOBIN STANDARDS

For a number of years a discrepancy has been noted in the hemoglobin standards of England and of America. The English standard was that of Haldane, and was based on the color of carbon monoxide hemoglobin. According to this standard the blood of the average man contains 13.8 gm. of hemoglobin per 100 cc. and has an oxygen capacity of 18.5 cc. American workers, using other methods for determination of oxygen capacity and hemoglobin,⁹⁹ found considerably higher values, namely, 15.8 gm. of hemoglobin and 20.9 cc. of oxygen per 100 cc.¹⁰⁰⁻¹⁰² The discrepancy was at one time attributed to the greater number of automobiles in the United States, which produced a mild degree of chronic carbon monoxide poisoning, with a resultant increase in hemoglobin.¹⁰³ Little support was found for these suggestions, and it was found that, when the Van Slyke method for determining oxygen content was employed, English blood samples showed higher hemoglobin levels than were given by the Haldane hemoglobinometer¹⁰⁴ and that high values could be obtained in other centers of population, such as Sydney.¹⁰⁵ With the arrival in England of American soldiers, it became apparent that there was no difference between the hemoglobin levels in the blood of English and American soldiers, and the reputed differences must have a methodologic origin. When the Haldane standard was re-examined by a new method for assay of hemoglobin,¹⁰⁶ it was found that in fact it corresponded to a hemoglobin content of 14.8 gm. and an oxygen capacity of 19.8 cc. per 100 cc.¹⁰⁷⁻¹¹⁰ "How it has come about," state one group of workers,¹¹⁰ "that this standard, which has been checked and rechecked for more than forty years, could have changed from an original equivalence of 18.5 ml. of oxygen to the present 19.8 ml. is a perplexing problem." They incline, however, to the belief that the fault lies primarily in the reliability of the Haldane method for gas analysis in blood. Whatever the cause, the English standard is now brought more closely in alignment with the American figures.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30411

PRESENTATION OF CASE

First admission. A fifty-nine-year-old executive entered the hospital for study.

The patient had been in fairly good health until three weeks before entry, when he experienced sudden, severe, generalized and persistent pain in the abdomen. There was no nausea or vomiting, changes in the number, the character or the color of the stools. The pain was unrelated to meals and lasted for nine days. It was relieved by warmth and aggravated by lying down. He had had no recurrence of the pain, no weight loss and no anorexia or night sweats.

He had been asymptomatic until four years before admission, when, because of pain on swallowing, he had had x-ray studies, which showed an esophageal hernia and diverticulum." Twenty years before entry, after a nine-month period of pain, a "duodenal ulcer" was demonstrated by x-ray. Since then he had experienced some subcostal distress after meals, especially after drinking alcoholic beverages and during episodes of nervousness.

Physical examination showed a well-developed, well-nourished man in no distress. The heart and lungs were normal. The abdomen was slightly distended, with slight tenderness in both flanks. The blood pressure was 130 systolic, 80 diastolic. His temperature, pulse and respirations were normal.

Examination of the blood showed a hemoglobin of 14 gm. The white-cell count was 12,200, with 9 per cent neutrophils. The urine was normal. The blood Hinton test was negative. One stool examination was negative. A phenolsulfonephthalein test, intravenous pyelograms and a barium enema were normal. A gastrointestinal series showed a moderate-sized hiatus hernia that emptied freely into the subdiaphragmatic part of the stomach. The stomach itself was otherwise negative. The duodenal cap showed a constant deformity, but no evidence of an active ulcer. A six-hour film showed the stomach completely empty; the head

of the meal was in the colon. He was discharged on the fourth hospital day.

Second admission (one year later). Following discharge the patient had occasional bouts of epigastric distress, characterized as dull, aching and heavy. These were associated with a constant dull pain in the right shoulder. There were occasional periods when he was unable to swallow. He had had no nausea, vomiting or loss of weight. About three months before re-entry the epigastric pain became more frequent and increased in severity. He experienced pain in the left shoulder similar to that on the right. He had had some constipation.

Physical examination showed a well-developed, fairly well-nourished man in no discomfort. The heart and lungs were normal. There was tenderness on deep palpation immediately under the xiphoid, but not elsewhere.

The blood pressure was 120 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,610,000, with 14 gm. of hemoglobin. The white-cell count was 7200. The urine was essentially negative. A gastrointestinal series showed no remarkable change in the hiatus hernia itself, but there was a constant area of narrowing just above the hernia. Barium passed through this region without much hesitation, but the area did not distend so completely as did the rest of the esophagus. The lumen was somewhat irregular in its course. The stomach was essentially negative. The duodenum showed evidence of an old ulcer deformity. On the first hospital day he had an attack of sharp epigastric pain lasting three hours. An electrocardiogram on the next day was normal.

On the third hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHESTER M. JONES: The pain that this man complained of was fairly characteristic of ulcer.

There are a lot of facts that are absent here and a lot of definite evidence that can be verified by looking at the series of x-ray films. There is no doubt that this man had a para-esophageal hernia. His symptoms were characteristic of it, although usually the pain of hiatus hernia is substernal rather than epigastric. It appears, however, that he had high epigastric and subxiphoid pain and occasionally pain in the right and left shoulders. If we take these statements alone, knowing that he had a para-esophageal hernia, the picture is entirely consistent. Of course a large number of patients with such a hernia have no symptoms. The fact that the pain went through to the back and radiated at times to one or the other shoulder and arm is also characteristic of many hernias.

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is fairly uncommon to find a combination of cancer and ulcer, and a hiatus hernia in addition even rarer. Because of the pain it was probably a benign lesion, since most esophageal cancers are not painful, and there is usually trouble with swallowing, described as a difficulty in getting food by a narrow spot. We must be prepared to be told that there was a carcinoma instead of a benign lesion, but I shall vote for a benign lesion, with partial stricture of the esophagus above the hernia. I still think he should have been esophagoscoped before operation, if it was possible.

DR. CASTLEMAN: Will you describe your operative procedure, Dr. Sweet?

DR. SWEET: First, I should like to comment about esophageal pain in these lesions, particularly the pain of cancer. Many of these patients do have a steady boring pain in the back, which usually is a sign of inoperability. In other words, transmission of pain almost never occurs until there is inflammatory fixation or invasion by the tumor. I am guided by that and by a persistent elevation of temperature in deciding whether a case is operable.

DR. JONES: This patient did not have fever or constant pain.

DR. SWEET: No; but he had a marked change in the character of the pain between the two admissions. I do not know whether or not that is brought out in the abstract. At the time of the first admission the pain was consistent with that of a hiatus hernia. Later, he had the pain of obstruction, and at operation it was quite obvious that he had an annular thickened mass in the lower portion of the esophagus. He had a hiatus hernia, as well as a short esophagus; in fact, he was one of the relatively few patients with a really short esophagus. The mass in the lower esophagus was adherent to the surrounding tissues and looked and behaved grossly like a carcinoma. I thought when I was removing it that I probably was taking out a carcinoma.

CLINICAL DIAGNOSIS

Esophageal (diaphragmatic) hernia.
Carcinoma or ulcer of esophagus?

DR. JONES'S DIAGNOSES

Hiatus hernia with short esophagus.
Peptic ulceration in esophagus or hernia.

ANATOMICAL DIAGNOSES

Hiatus hernia with short esophagus.
Peptic ulcer of esophagus.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The specimen we received was composed of the lower portion of the esophagus and a small portion of the stomach. With the aid

of Dr. Sweet we were able to delimit the part of the specimen that was above the diaphragm and that which was below. Everything below the diaphragm comprised normal stomach. In the center of the portion above the diaphragm was a large ulceration, surrounded by islands of mucosa that proved histologically to be gastric epithelium. We cut four or five sections at various levels, and even in the most proximal section we found a few small islands of stomach epithelium and a few of esophageal epithelium. Microscopically the ulcer had a fibrinoid base characteristic of peptic ulcer.

This case brings up the old question whether the presence of gastric epithelium above the diaphragm means a short esophagus with a portion of normal stomach below it, or whether the gastric epithelium is merely ectopic within an esophagus of normal length. The presence of this amount of gastric epithelium high in the esophagus certainly favors the short-esophagus theory.

The peptic ulceration was undoubtedly caused by the action of the hydrochloric acid secreted by the gastric epithelium on the adjacent epithelium, either gastric or esophageal, or both. I do not see how we can decide the point because we cannot tell what type of epithelium it was before it was ulcerated. My hunch is that both were ulcerated. There was no evidence of carcinoma.

DR. SWEET: This case is extremely instructive. The increasing possibility of the surgical management of lesions in this region of the body brings to my mind the analogy between this lesion and a prepyloric ulcer. I believe that both should be handled clinically in exactly the same way. In other words, I could not tell preoperatively or at the time of operation whether I was dealing with carcinoma or a benign ulcer. The same thing holds true in a prepyloric lesion. Both should be regarded with great suspicion. These esophageal lesions should be resected, because the operative mortality is now down to a perfectly reasonable level, comparable to that of gastric surgery through the abdominal approach.

DR. JONES: Furthermore, it is also true that even if they do not carry so high an incidence of carcinoma as do the prepyloric ulcers, lesions like this are bound to give stenosis before long.

DR. CASTLEMAN: I have been under the impression that most peptic ulcers of the esophagus heal without stenosis. Do you know, Dr. Holmes?

DR. HOLMES: We see so few that I do not know.

I should like to add that this case has brought out an interesting problem in connection with radiology of that part of the body. I have a suspicion that the congenital short esophagus is much more frequent than we had thought it was. I assume that those with the short esophagus are likelier to have regurgitation of food or gastric

I am not at all certain about the diverticulum; it is described clearly at first but is not mentioned on subsequent x-ray examinations. If he had one, it was at the cardiac end of the esophagus. Diverticula may or may not be asymptomatic. One might add that in an esophageal hernia that gives symptoms the esophagus usually shows either local change in the lower end or a true gastritis in the hiatus hernia. In many cases it is worth while to do gastroscopy and esophagoscopy to localize the site of the irritating process.

This man had an ulcer demonstrated by x-ray twenty years before admission. The x-ray films that were taken a year ago and the current ones do not mention ulcer activity in the sense that a crater was visualized. The story as given here is not that of active ulcer unless we say that the last episode—the sharp attack of epigastric pain and so forth—meant a perforation; and then we are at a loss because we know nothing about the physical examination at the time of the last admission. We do not know whether he had epigastric spasm and local tenderness, and there is no information about the episode that led to operation. It is fair to assume that because operation was done on the third hospital day it was thought that he had not a cardiac but a gastrointestinal lesion as the cause of pain. Surgical intervention would be warranted for two or three reasons. One would be an acute perforated ulcer either in the duodenal cap, where it had been localized before, or in the esophagus, just above the herniation or in the herniation itself. An esophageal ulcer is relatively rare. He might have had an incarcerated hiatus hernia that required surgery but this is also an uncommon occurrence, and one would not expect it with a hernia of this size that emptied on both occasions by x-ray. I do not believe that such was the reason for surgical interference. The third reason, which might have had nothing to do with the sharp attack of epigastric pain, is narrowing at the lower end of the esophagus. This suggests intrinsic disease of the lower esophagus due to an inflammatory process around an ulcer or a carcinoma without many symptoms to call attention to it.

At this point I think it would be worth while to go over all the x-ray films to see if anything more can be made out of them, remembering that the surgeon rarely operates on hiatus hernia and esophageal ulcer and also that the clinical picture given is not that of an acute perforation of a duodenal ulcer.

DR. GEORGE W. HOLMES: I have no films to show the diverticulum of the esophagus.

DR. JONES: And it was not mentioned in the fluoroscopic note?

DR. HOLMES: If you do not mind, we shall forget about it.

DR. JONES: I should like to because I do not believe that a diverticulum was present.

DR. HOLMES: This film represents the examination of the colon and is essentially negative. I have been through the films taken of the duodenum; there is a deformity but at no time were we able to demonstrate a crater, and there is nothing in the films to suggest hyperperistalsis. It seems unlikely that the finding was due to an acute duodenal ulcer. The lesion that seems to me to be the most significant is the hiatus hernia, with the esophagus coming in at its top. That is of some importance because it is in these cases of so-called "short esophagus" that ulcerations in the esophagus are likely to occur.

Then we have the films that show the actual lesion in the esophagus. There is a defect that looks like an ulcer crater. I remember this case, and I think that that was interpreted as a benign ulcer of the esophagus.

DR. JONES: In other words, this is not the usual case of para-esophageal hernia but represents the smaller group of cases with a short esophagus. The symptoms can be entirely explained by what we see in the x-ray films. The patient had a hernia and there was a lesion above it in the anterior portion of the esophagus, which was due to inflammatory disease or to an infiltrating process. This is the sort of case that should be esophagoscopy before any surgery is attempted. Was an esophagoscopy done?

DR. BENJAMIN CASTLEMAN: No.

DR. JONES: It may have been impossible because of the emergency that arose on the third hospital day,—the three-hour attack of sharp epigastric pain,—and the surgeons may have thought that it was wiser to operate than to try to establish a diagnosis. A diagnosis could probably have been established by careful esophagoscopy.

I should like to ask what the belly was like after this episode of pain. Was there anything to suggest a perforated ulcer?

DR. CASTLEMAN: Dr. Sweet, can you answer that?

DR. RICHARD H. SWEET: No; I did not see the patient during that attack of pain. When he came in the second time he was having pain, but it was not that of peritoneal irritation.

DR. JONES: That statement modifies the picture. The record states that there was an attack of pain lasting three hours on the day of admission, which may be a little misleading.

DR. SWEET: The pain was induced by eating, and it was rather constant.

DR. JONES: I do not believe that the duodenal ulcer had anything to do with the picture, nor do I believe that the patient had a perforation that warranted surgical interference. The acute or subacute portion of the story probably represents pain arising from an active ulcerated lesion above the hiatus hernia. I do not know whether it was due to cancer or to a peptic ulcer of the esophagus.

DIFFERENTIAL DIAGNOSIS

DR. FLETCHER H. COLBY: In the first admission there is a long history of pain in the lower abdomen and of backache, with a hospital admission in which the essential findings were fever, leukocytosis, lower abdominal tenderness and evidence of peritoneal irritation. At that time a mass was felt in the left side of the pelvis and there was evidence of inflammation of the glands of Skene and Bartholin. With bed rest, intravenous fluids and chemotherapy this acute illness subsided. A reasonable explanation for this episode seems to be an acute flare-up of a pelvic inflammation.

In about two months the patient returned to the hospital with pain and tenderness in the lower abdomen, and what I should suppose was a recurrence of the low-grade pelvic inflammatory process. At that time there was no fever or leukocytosis, and there was but little abdominal tenderness. There were, however, costovertebral tenderness on the left and hematuria. I assume that the hematuria was total, and that the urine was grossly red.

DR. RONALD C. SNIFFEN: Yes.

DR. COLBY: Considerable blood was present in a catheterized specimen of urine. The previous urine was acid, with a low specific gravity and a few pus cells. Evidence that was obtained by cystoscopic, x-ray and pyelographic examinations strongly suggests that the left kidney was the source of the bleeding. At least no note was made of a tumor in the bladder or of any acute inflammatory process of such magnitude as to result in obvious bleeding. Gross bleeding in the urinary tract in the majority of cases — at least 70 per cent — is due to stone, tumor or tuberculosis; in approximately 25 per cent it is due to nontuberculous inflammatory lesions, and in the other odd 5 per cent it is caused by various blood dyscrasias and so forth. So I think that we can fairly assume that this woman had a process in the left kidney that was one of the first three possibilities.

Is there any way of connecting the previous entry with the second entry and the left renal lesion? She might have had a tuberculous pelvic inflammatory process all the time, and it is possible that the left kidney was the site of a primary tuberculous lesion that gave a filling defect. Such lesions are the rare tuberculomas that are found sometimes in the kidney and occasionally in the bladder. It hardly seems likely that this woman had tuberculosis because of the lack of persistent severe bladder symptoms and the lack of any described bladder or vesical changes on cystoscopic examination. So it seems reasonably certain that the pelvic inflammatory disease and the renal disease were two separate things. The diagnosis of the lesion in the left kidney depends entirely on the interpretation of the pyelogram.

DR. MILFORD SCHULZ: This is the film made thirty minutes after the intravenous injection of the dye. You can see the large right kidney and the large left kidney, which has only a little dye in the calyces. This is the shadow thought to be a stone, but on the retrograde pyelogram it is shown to be outside the ureter. The upper calyces are not greatly dilated, but there is a mass projecting from the lateral margin of the left kidney that can almost be traced around the defect in the pelvis and that deforms the middle and lower calyces.

DR. COLBY: Will you look at this flat film and tell me if there is any irregularity of the renal outline.

DR. SCHULZ: Yes; on the left side. You can see it here on the retrograde film. I do not see any evidence of metastases in the bones.

DR. COLBY: The filling defect in the lower end of this kidney seems to be the important sign.

What are the possibilities? In the first place, it might have been a nonopaque stone; in the second place, a tumor of some sort — neoplasm or a blood clot. Nonopaque stone is a difficult diagnosis to make. Air pyelograms are helpful in the majority of cases, as in those of uric acid stone, but at times one cannot diagnose a stone by any means we have of visualization of the interior of the kidney. There is no evidence of calcification in the plain film in this region, and the patient's history somehow does not suggest the presence of nonopaque calculus. Renal pain had not been severe or significant in the history. It was an acute episode accompanied by profuse gross hematuria.

This story suggests a malignant tumor of the left kidney. There are two varieties of tumors — those that arise from the parenchyma and those that arise from the renal pelvis. If we say that it was a neoplasm involving the left kidney, which one was it? My experience with tumors primary in the renal pelvis has been that they involve the pelvis, and the pelvis in this case does not seem to have been involved. I have never seen a primary tumor of the pelvis of the kidney involve a localized area, such as one calyx, but I suppose that it is possible. Against that is the lack of function of this kidney. Function as a general thing was poor from the left kidney, which suggests, not a localized tumor of the renal pelvis, but a tumor involving the parenchyma. Such tumors, as a rule, are renal-cell carcinomas.

DR. OLIVER B. COPE: You exclude an infection, such as tuberculosis?

DR. COLBY: There is no report of a culture.

DR. COPE: What about the x-ray findings?

DR. COLBY: I have to take the evidence that is given.

DR. FULLER ALBRIGHT: Could it have been a polycystic kidney?

juice into the esophagus. We know that ulcer frequently occurs in cases of hiatus hernia with a short esophagus, and we should look more carefully for small esophageal ulcers in these cases. I have seen a number of cases in which the esophagus immediately above the hernia looked narrowed but I have not studied this area with sufficient care. I believe that we are going to be in a position to make better diagnoses in this group. It would be interesting to review the cases in which the patients have had pain to see what type of hernia they had and also to see how many had an ulcer in the esophagus.

CASE 30412

PRESENTATION OF CASE

First admission. A thirty-eight-year-old housewife entered the hospital because of acute epigastric pain.

For about eighteen years, that is, since the birth of her first child, the patient had recurrent attacks of "burning pain and a heavy feeling" in the lower abdomen associated with soreness in the lower back. She had had occasional dysuria, but no nausea, vomiting, fever or chills. The pain gradually increased in severity and frequently occurred while she was in bed. It was increased by coughing, but not by straining, and occasionally preceded menstrual periods. Eighteen months before entry she had an attack of severe, crampy pain in the right upper quadrant, which lasted intermittently for four days. There was considerable vomiting, and frequent headaches. A Graham test was negative. The pain disappeared after four days, but she continued to have gaseous eructations after eating fatty foods. Five days prior to admission the patient began to have severe pain in the lower abdomen and back, which was intermittent until the day before entry, when it became steady. She had dysuria and felt warm, but there had been no chills.

Physical examination showed a well-developed, rather obese woman in some distress. The lungs were clear, but the bases appeared high and the diaphragmatic excursions were limited. The heart was normal. Diffuse tenderness was present over the entire abdomen, most marked in the lower quadrants, where there was rebound tenderness. Peristalsis was normal. Pelvic examination revealed a whitish vaginal discharge. Shotty Skene's and Bartholin's glands were present. The cervix was lacerated and freely movable. One examination revealed a 3-cm. mass in the left vault. There was tenderness in both vaults, more marked on the left.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 102.8°F., the pulse 85, and the respirations 20.

Examination of the blood showed a white count of 11,800. The urine was cloudy, and the sediment contained occasional white cells. A blood Hinton test was negative. A smear of the cervix discharge showed questionable gram-negative cocci but a culture was negative for gonococcus.

The patient was Ochsnerized and given 3000 cc. of 5 per cent dextrose in physiologic saline solution for four days and 6 gm. of sulfadiazine daily for seven days. The pain, tenderness, nausea and vomiting subsided and she was discharged on the eleventh hospital day.

Second admission (about two months later). After discharge she was well for one month, which time the lower abdominal pain and tenderness recurred. There was pain in the left flank and the costovertebral angle, radiating to the suprapubic region and up to the left shoulder. The character of this pain and its relation to the lower abdominal pain were not recorded. Three days before entry she developed persistent hematuria.

Physical examination showed a normal heart and normal lungs. Slight tenderness was elicited on palpation of the abdomen. Tenderness and sense of resistance were present in the left flank but no masses were palpable. Pelvic examination revealed some tenderness but no masses.

The blood pressure was 152 systolic, 94 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a white count of 9000, with 12.8 gm. of hemoglobin. The urine was acid, with a specific gravity of 1.008 and a + test for albumin; the sediment contained 60 white cells, 25 epithelial cells and rare red cells per high-power field. A second (catheterized) specimen contained numerous red cells. The nonprotein nitrogen was 26 mg. per 100 cc.

A plain film of the abdomen showed both kidneys to be large. The left kidney was somewhat lower than the right. There was a small area of calcification 3 cm. below the level of the left sacroiliac region. An intravenous pyelogram revealed prompt excretion of the dye by the right kidney outlining a nondilated pelvis, calyces and ureter. Only an extremely small amount of dye was visible in the region of the calyces of the left kidney and there was no further evidence of dye in 30 minutes. The left ureter was not visualized. The outline of the left pelvis and calyces was so faint that no conclusion could be drawn. Retrograde pyelograms of the left kidney showed the calcified area to be outside the ureter. The left ureter, pelvis and superior calyces filled normally. The lateral branches of the lower calyx were dilated, with loss of normal cupping. In one of the films a filling defect was seen in this calyx. X-ray films of the chest were negative.

On the tenth hospital day an operation was performed.

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TREATMENT OF MENINGOCOCCAL MENINGITIS

In few conditions have the sulfonamide drugs proved of greater value than in certain types of bacterial meningitis, particularly meningococcal meningitis. The case fatality rate of epidemic meningitis was about 40 per cent in Army camps during World War I, in spite of the fact that intensive treatment with antimeningococcus serum was used. During the present war the over-all mortality from this disease in the Army and Navy is well under 5 per cent, and in several large posts 100 or more consecutive cases have been treated with fatality rates of 2 per cent or less. Further-

more, there has been a remarkably low incidence of complications.

These brilliant results have been obtained with a relatively simple treatment—the oral administration of sulfonamide drugs, supplemented when necessary in severe cases by the intravenous injection of their sodium salts.¹ This is in contrast to the traumatic and cumbersome methods formerly used—the intravenous and intrathecal injection of serum. Antimeningococcus serums are still used by some medical officers and civilian physicians, perhaps because they prefer to cling to tradition or because they assume that serum therapy is an essential part of “doing everything possible.” There seems to be little, if any, reason for believing that this supplementary form of therapy is of additional benefit. Indeed, there is increasing evidence that antimeningococcus serum, particularly when given by the intrathecal route, may actually do more harm than good in most drug-treated cases.

The sulfonamides have also been highly effective in the management of meningococcus carriers, particularly the mass elimination of such carriers from large military units. The latter can be accomplished by a single dose or by one short course of a few grams of a sulfonamide drug given orally in a single day and is, likewise, in sharp contrast to the cumbersome, and usually unsuccessful, methods employed during World War I.

Drug-fastness is a serious problem in the sulfonamide treatment of infections with the gonococcus, an organism that is closely related biologically to the meningococcus, and increasing numbers of sulfonamide-resistant cases of gonorrhea are constantly being encountered in all parts of the world where these drugs are widely used. Among the sulfonamide-treated cases of meningococcal meningitis there have been some failures, particularly in fulminating acute cases and in late and neglected ones. There have also been some apparent failures, owing to the improper control of therapy, which vitiated or obscured the beneficial effects of the drug. There have been few, if any, authentic cases, however, in which the sulfonamide resistance

DR. COLBY: It was unilateral; I have never seen a case of unilateral polycystic disease, although they have been reported. In the x-ray films there is nothing to suggest to me that a bite had been taken out by a cyst. The defect is irregular, suggesting a tumor or blood clot.

CLINICAL DIAGNOSIS

Renal tumor.

DR. COLBY'S DIAGNOSIS

Renal-cell carcinoma.

ANATOMICAL DIAGNOSIS

Polycystic kidney.

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: The specimen proved to be a polycystic kidney. It was of normal contour, as most of them are, and about twice the normal size. Externally and internally it was riddled with cysts, so that there was little parenchyma—just two or three islands of recognizable cortical tissue. The pelvis and calyces were dilated, but not greatly distorted. I do not believe that this kidney explains all the patient's symptoms; in all probability the first symptoms were due to pelvic inflammatory disease.

DR. ALBRIGHT: What was the x-ray diagnosis?

DR. SNIFFEN: Neoplasm of the left kidney.

DR. COLBY: And the preoperative diagnosis?

DR. GEORGE G. SMITH: I operated on this patient, and the preoperative diagnosis was renal tumor.

DR. COLBY: That makes me feel better.

DR. SNIFFEN: The cause of death in patients with polycystic kidneys is assumed to be a gradual enlargement of the cysts without increase in num-

ber, with consequent atrophy of the remaining parenchyma. In a few cases, however, there is the added factor of hypertension, following vascular changes in the kidney. In such cases, renal failure can be explained, at least in part, by severe nephrosclerosis.*

DR. LLOYD MILLS: In the absence of more information about the urine, what do you think was the cause of the pain?

DR. SNIFFEN: Several things may cause pain among them hemorrhage into a cyst and clotting of blood in the ureter.

DR. SMITH: A cyst will rupture into the pelvis. I have seen it happen with a solitary cyst, producing hematuria and a filling defect, a picture similar to that in this case.

In my operative note I said that the reason for removing the kidney was that the function was poor. It was obviously polycystic disease at operation. The other kidney was apparently carrying on the work. The blood nonprotein nitrogen was normal, and I thought that the patient would get into further trouble if the kidney were left in.

DR. SNIFFEN: The chances are that there was at least some degree of polycystic disease on the other side.

DR. SMITH: That may be true. On the other hand, a patient from whom I removed a polycystic kidney twenty years ago is still in excellent health.

Years ago we used to have a great deal of argument in the American Urological Association about polycystic disease. One member maintained that polycystic disease was unilateral as frequently as bilateral. A number of cases were discussed.

DR. SNIFFEN: Unilateral polycystic kidney does occur, but such cases are far in the minority.

DR. SMITH: Not over 5 per cent, I should say.

*Ritter, S., and Bachr, G. Arterial supply of congenital polycystic kidney. *J. Urol.* 21 583-592, 1929.

MINIMUM CURRICULUM AND SYLLABUS FOR SCHOOLS OF NURSING

THE Massachusetts Authority for Schools of Nursing has just issued a booklet to guide nursing schools in the construction of their curriculums. In the preface it is explained that this represents the joint effort of representative physicians and nurses to agree on what should be included in the ideal course of nursing. The impossibility of devising an inflexible statement of what should be included and what should be deleted is recognized, and is met by placing an asterisk opposite the subjects that are deemed most important. This, of course, represents a compromise between the thinking of those who wish to elevate the profession of nursing onto higher and more scientific levels and those who wish to extend its practical applications over a wider field of availability and usefulness — two aims that are quite diverse.

The same controversy exists in medical education: there are those who would exalt science and research exclusively and those who think that doctors should be trained merely to care for the sick population. Neither of these attitudes should be permitted to develop to any extreme degree or to the exclusion of the other. It is true that the outstanding individuals in any profession rise by their own innate aptitudes fully as much, or more, than by the schooling to which they are exposed. Without the schooling, on the other hand, they lack the sanction of authority — they are "irregulars," if such a noun is permitted, and there are irregulars in both camps.

The syllabus represents a nice balance between these educational elements. It will undoubtedly be a most useful and much-needed guide to those who are interested in the training of nurses, but it will naturally need periodic revisions and occasionally rewritings. The *Journal* welcomes it as an unusually competent statement concerning an important educational problem.

MISCELLANY

NOTE

The Board of Overseers of Harvard College at their regular meeting on September 25 approved a recommendation of the Faculty of the Harvard Medical School that women students be hereafter eligible for admission to the school. The recommendation had been previously approved by the Harvard Corporation and will become effective for students entering the school in the fall of 1945.

CORRESPONDENCE

BASAL TUBERCULOSIS

To the Editor: It was with great pleasure that I read the article by Dr. Emil Z. Ossen in the June 8 issue of the *Journal*. He treated the subject of basal tuberculosis in a masterful manner because the disease, being as uncommon as it is, often presents an annoying diagnostic problem. I might mention that we have seen a few cases over here that exemplified the material presented by Dr. Ossen.

At present, we have a young soldier of twenty-three who has basal tuberculosis in the upper portion of the left lower lobe. He, of course, will be sent back to the United States shortly. A history of familial contact, the physical findings, x-ray slides and the laboratory evidence are conclusive. When seen on sick call a few days ago, he presented only a few signs of pathology, namely, a low-grade fever (99.5°F.) and a few localized subcrepitant rales below and medial to the lower angle of the scapula. He felt quite well systemically — no lassitude, apathy or weakness. He was somewhat apologetic for coming on sick call. He had no history of anorexia, loss of weight, hemoptysis, night sweats or other evidence of tuberculosis. His history was one of parental exposure fifteen years previously, and none since then. Atypical pneumonia was believed to be the diagnosis when he was admitted to the hospital. Sputum taken immediately to the laboratory proved positive for tubercle bacilli. X-ray films showed a basal lesion, and none in the apex. A cavity was seen in the involved area. I should call this a "pure type." It is a fulminating type, I believe, in view of the lack of prodromal symptoms and the positive sputum. Frankly, I consider this type of tuberculosis somewhat terrifying because I believe that its detection can, at times, be extremely difficult. As mentioned in Dr. Ossen's article, bronchiectasis, neoplastic disease, pulmonary abscess and even mycoses can be ruled out rather easily most of the time. I am not quite so certain about atypical pneumonia, especially if negative sputums are obtained, as they are often at the onset of the disease. Pneumonitis certainly can appear on x-ray examination at a situation similar to that of the earliest stage of basal tuberculosis.

So far as the diagnosis of atypical pneumonia goes, over here we see far more unilateral than bilateral involvement, at least in the severe forms, which are not infrequent. Most of the medical officers here believe that this disease is transmitted from person to person by the usual droplet method, a theory that is not generally accepted by the profession. Furthermore, most of these patients show few physical signs for two or three days, and these usually are a few localized rales and nothing else. X-ray films show a picture similar to that of pneumonitis. Most of the patients stay in the hospital with a low-grade fever for two or three weeks. Treatment, of course, is symptomatic. Atypical pneumonia as seen over here certainly must be ruled out in these cases.

A final word about tuberculosis. I believe that a young person with long-continued fever and minimal pulmonary involvement has a graver prognosis than an older person with extensive involvement but with little fever. This is not exactly my own idea, but it has been impressed upon me during my tenure in the Army.

In conclusion, the matter brings out the old axioms and rules for practicing good medicine — CAREFUL HISTORY, CAREFUL PHYSICAL EXAMINATION, and CAREFUL AND COMPLETE LABORATORY EXAMINATION.

I. ROBERT FRANK
Major, Medical Corps, A.U.S.

Southwest Pacific Area

BOOK REVIEWS

The Inner Ear, Including Otoneurology, Otorrhinology, and Problems in Modern Warfare. By Joseph Fischer, M.D., and Louis E. Wolfson, M.D. 8°, cloth, 421 pp., with 77 illustrations and 7 tables. New York: Grune & Stratton, 1943. \$5.75.

This book, considering the senior author's excellent record as a teacher and contributor in this particular subject, fails to accomplish what the aim expressed in the preface — a simplified discussion of the inner ear. The fault does not lie with the contents of the book but mostly in the manner in

of meningococci obtained from human cases was bacteriologically proved.

With the introduction of penicillin and the demonstration of its effectiveness in the treatment of various infections, it was natural to explore its potentialities in all fields. The good results obtained with sulfonamides and the limited supply of penicillin did not permit early and extensive trials of the latter agent in meningococcal infections. Hence, only a small number of cases were included in the first extensive reports covering the clinical use of penicillin. In spite of the small number, it was evident that the results obtained with penicillin in meningococcal meningitis were not dramatic and that failures were encountered, particularly in cases in which sulfonamides had not been used.

Elsewhere in this issue of the *Journal* there is a report of an intensive study of a small group of cases of meningococcal meningitis treated with penicillin alone. The bacteriologic as well as the clinical results in these cases were quite disappointing when compared with those usually obtained with sulfonamides. So far as it is now known, cases of meningitis require intrathecal as well as parenteral treatment with penicillin to control the meningeal infection. This is accompanied by a definite and not insignificant inflammatory reaction, manifested by an increase in the pleocytosis of the spinal fluid and often by exaggeration of the signs and symptoms of meningeal irritation. These reactions are undesirable and often harmful, since they may interfere with the prompt bacteriologic cure and may prolong and aggravate the clinical symptoms. The parenteral and intrathecal use of penicillin, and even its use as a spray, have apparently failed also to rid the nasopharynx of meningococci.

The results in this series of cases were obtained with doses of penicillin that are usually considered to be adequate and in cases in which care had been taken to eliminate any effect of sulfonamides. The authors found out that the latter — that is, the exclusion of sulfonamide therapy — is essential in evaluating the effect of penicillin in cases of meningococcal infection.

Some good results following the use of penicillin in experimental and clinical meningococcal infections have been recently reported. Experimental infections, however, are not comparable to clinical cases of meningitis; moreover, the results were not nearly so good as those obtained in experimental infections with other organisms, such as pneumococci and streptococci. In the clinical cases, as previously stated, the actual role of the penicillin cannot be evaluated unless the effects of sulfonamides are excluded. Unfortunately, this point is not stressed in these reports — for example, that of Rosenberg and Arling.² There, it is stated that the only fatal case in the series did receive a sulfonamide drug. Furthermore, the fact that negative primary cultures and smears of the spinal fluid were obtained in 15 of the 65 cases strongly suggests that a sulfonamide had been given in these 15 cases and perhaps in many of the other cases before the initial dose of penicillin.

For practical purposes it may be said that sulfonamide drugs still constitute the treatment of choice in meningococcal meningitis. Penicillin therapy is more laborious, more traumatic and more expensive, in addition to being less effective in curing the meningeal infection and in eliminating the carrier state. From the information thus far available it seems wise to reserve penicillin for use as an adjunct to the sulfonamide drugs in those cases in which the latter do not bring about an adequate clinical response or for use in cases in which sulfonamide drugs cannot be given. Penicillin may also prove helpful in the management of focal purulent meningococcal infections, particularly those of the joints. Withdrawal of synovial fluid and intra-articular injection of penicillin may hasten the bacteriologic cure of such infections. It is not clear from present reports whether the clinical results of the use of penicillin in such focal complications are superior to those observed with sulfonamides.

REFERENCES

1. Finland, M., and Dingle, J. H. Treatment of meningitis. *New Eng. J. Med.* 225:825-832, 1941.
2. Rosenberg, D. H., and Arling, P. A. Penicillin in treatment of meningitis. *J. A. M. A.* 125:1011-1016, 1944.

Elements of Medical Mycology. By Jacob H. Swartz, M.D. With an introduction by Fred D. Weidman, M.D. 8°, cloth, 9 pp., with 78 illustrations. New York: Grune and Stratton, 1934. \$4.50.

This excellent elementary text, covering the organisms commonly encountered in the United States, fills a distinct void in medical mycology. In the general discussion, the principal morphologic characters are defined and accompanied by line drawings; the commoner genera are listed with the organs usually attacked and the names of the diseases produced. This is followed by a detailed account of the laboratory methods for the confirmation of the clinical diagnosis that the author has found most useful in his practice. The chapter on the yeast-like fungi is largely clinical and therapeutic, with little detail on the organisms involved beyond the information necessary to refer them to this group. The trichophytons producing various tinea are treated in much more detail. Blastomycosis (Gilchrist's disease), coccidioid granuloma, chromomycosis, sporotrichosis, actinomycosis, tinea versicolor and histoplasmosis are grouped in a chapter of miscellaneous organisms, followed by a short chapter on common contaminants. A brief chapter on immune reactions and one on the effects of sulfanilamide and its derivatives, an extensive glossary and a folding chart presenting the salient features of the book in tabular form complete the work.

Although this book may seem oversimplified to the specialist in this field, it should prove a valuable text for the beginner and for the busy clinician. It is unfortunate that the author has placed the organism of Gilchrist's disease among the Blastomyces in violation of the international rules of botanical nomenclature and has confused the clinical pictures of Brazilian blastomycosis caused by *Paracoccidioides brasiliensis* and by *P. cerebriiformis*. The illustrations of lesions are well chosen, and the photomicrographs of the organisms are excellent.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Handbook for the Medical Secretary. By Miriam Bredow, dean of women, Eastern School for Physicians' Aides. 8°, cloth, 253 pp., with 18 illustrations. New York: McGraw-Hill Book Company, Incorporated. 1934. \$2.25.

This manual is written for medical secretaries who are already employed and also as a text for students training for the various phases of work to be found in the office of a physician. A valuable vocabulary of approximately 2000 medical terms is appended to the text. Pronunciation is given for the words uncommon to the layman. The vocabulary is divided into subjects, and would be more useful if it had been arranged in one alphabet.

The Permeability of Natural Membranes. By Hugh Davson, D.Sc., associate professor of physiology, Dalhousie University, Halifax, Canada, and James Frederic Danielli, D.Sc., A.I.C., Beit Memorial Research Fellow and Fellow of St. John's College, Cambridge, England. With a foreword by E. Newton Harvey, Ph.D., professor of physiology, Princeton University, 8°, cloth, 361 pp., with 73 illustrations and 72 tables. New York: The Macmillan Company, (Cambridge, England: University Press), 1943. \$4.75.

The authors have brought together in this volume the existing knowledge of cell permeability.

Traumatic Injuries of the Facial Bones: An atlas of treatment. By John B. Erich, D.D.S., M.D., consultant in laryngology, oral and plastic surgery at the Mayo Clinic, and assistant professor of plastic surgery, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota; and Louie T. Austin, D.D.S., head of Section on Dental Surgery at the Mayo Clinic, and associate professor of dental surgery, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota. In collaboration with Bureau of Medicine and Surgery,

United States Navy. 12°, cloth, 600 pp., with 333 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. \$6.00.

The present war has shown a decided increase in serious facial injuries, the treatment of which is becoming more and more complex. The large experience of the authors at the Mayo Clinic has been drawn on in presenting treatment for the various types of injuries of the facial bones. The major portion of the work is given up to a discussion of fractures of the facial bones. A small portion is devoted to bone and skin grafting, wiring and splinting.

An Atlas of Anatomy. By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.), professor of anatomy, University of Toronto. Volume II. *Vertebrae and cerebral column, thorax, head and neck.* 4°, cloth, 184 pp., with 232 illustrations. Baltimore: The Williams and Wilkins Company, 1943. \$5.00.

This is the concluding volume of an atlas designed to meet the needs of teachers and students, physicians and surgeons. The regional presentation, which is based on American methods of dissection, makes the atlas of permanent value in clinical work. The illustrations were taken from actual specimens, and the accuracy of the plates was checked by photographic means. The observations and comments that accompany the illustrations are not exhaustive descriptions but are designed to attract attention to salient points that might otherwise escape notice. The color work is good, reminding one of the best German atlases.

Education and Health of the Partially Seeing Child. By Winifred Hathaway. A publication of the National Society for the Prevention of Blindness, Incorporated. 8°, cloth, 216 pp., with 34 illustrations and frontispiece. New York: Columbia University Press, 1943. \$2.50.

This valuable monograph on a sociologic subject is of great importance to the community, since it has to do with the child who is usually a misfit in the public schools. Mrs. Hathaway is an authority on blindness and in this book explains the principles underlying educational procedures and health service for partially seeing children and shows that they may be applied to further the education and health of these children wherever they may live. She describes specifically the equipment, mechanical devices and teaching methods that are available and also discusses the various problems of classification, supervision and financing that are involved in an education program for partially seeing children. The book is designed for all persons, including parents, who are responsible for the partially seeing child. It is interesting to note that the first class in the United States established especially for partially seeing pupils was inaugurated by the Boston School Committee in 1913. This text should serve as an authoritative reference source on its subject.

On the Influence of Trades, Professions and Occupations in the United States in the Production of Disease. By Benjamin W. McCready, M.D. With an introductory essay by Genevieve Miller, M.A. 12°, cloth, 129 pp. Baltimore: The Johns Hopkins Press, 1943. \$1.75.

The text of McCready's prize dissertation, originally published in New York City in 1837, is reproduced in full. In the introduction, Miss Genevieve Miller, assistant at the Institute of the History of Medicine, Johns Hopkins University, comments on the conditions of industry in the United States at the time of McCready's dissertation. She also discusses briefly the life and work of McCready and proceeds to analyze his monograph. In preparing his essay on occupational diseases in America, McCready endeavored to obtain information on the subject by writing letters and interviewing workmen but without much success. He also tried to consult the books of various trade organizations to find material on mortality rates, but again was disappointed since there were no records at all or only imperfect ones. Therefore, with such scanty material he depended rather extensively on a book by Thackeray on occupations, published in London in 1851. He included also personal observations made when he was house physician at the New York Hospital. Miss Miller characterizes the McCready essay as the first American treatise on occupational diseases. Thirty-one types of employment, divided into four sections, are discussed, and in her introduction she points out those details that are additions to the previous literature. She concludes that the essay was a remarkably mature and realistic ap-

which it was printed and illustrated. The illustrations, particularly the photographs of temporal bone and skull, are not well reproduced. The reader therefore misses much of the subject matter because of the lack of comprehensive illustrations. The experienced otologist will enjoy reading the chapters dealing with physiology and anatomy, which are interestingly presented.

There is a definite need for a treatise of this kind for otologists, neuro-otologists and neurosurgeons. In the next edition the authors in all probability will overcome these not too serious defects.

A Clinical and Experimental Investigation of the Blood Cholesterol Content in Myxedema and Other Conditions. By E. H. Stokes, M.B., Ch.M. (Sydney), F.R.A.C.P. 4th, cloth, 121 pp., with 13 illustrations. Sydney: Australasian Medical Publishing Company, Limited, 1941.

The writer of this monograph happened to become interested in cholesterol metabolism through seeing a patient with myxedema and hypercholesterolemia. This was nineteen years ago. Ever since then the riddles of cholesterol metabolism have fascinated him, and in 1928 he began to attempt to solve them by systematic study.

The result of all the work that he has done in this field is now printed. The author writes easily, so that what he says is well expressed. He is a good student of literature, so that he has compiled a useful bibliography. He is conservative in his conclusions, so that he modestly admits there still are many undiscovered factors other than a deficiency of thyroid that may play a part in producing hypercholesterolemia in myxedema.

On the whole this book will prove a useful one for reference. It is especially pleasant to welcome it as a fair sample of the type of medical investigation now going forward in the laboratories and wards of our Australian colleagues.

Strabismus. Its etiology and treatment. By Oscar Wilkinson, M.D., D.Sc. In collaboration with Richard W. Wilkinson, M.D., M.Sc. (med.). Second edition, revised. 8th, cloth, 369 pp., with 71 illustrations. Boston: Meador Publishing Company, 1943. \$4.00.

The second edition of this book, with the chapters on non-surgical and surgical therapy largely rewritten, and with ample recognition and citation of authorities throughout the text, offers an ideal review of the problems in strabismus for the young ophthalmologist.

Adequate attention is given to etiology and types of strabismus, to methods of examination of the patient, and to non-operative and operative therapeutic procedures and their indications. The text is concisely and interestingly written and is amplified by numerous illustrations and drawings. Forty pages are devoted to illustrative cases, with essential items from the case history, and photographs before and after treatment.

Life Is Too Short: An autobiography. By C. Kay-Scott (Frederick Creighton Wellman, M.D.). 8th, cloth, 348 pp. Philadelphia: J. B. Lippincott Company, 1943. \$3.50.

Dr. Frederick Creighton Wellman, also known under the name of C. Kay-Scott, is one of the few people who appears in *Who's Who in America* under both names. He has led a most extraordinary life and his volume of reminiscences is an interesting autobiography of a man of many careers.

His grandfather, a physician born in Virginia, served in the Civil War on the Confederate side. He later moved to Missouri, where the author was born in Independence. His father became a missionary to Indian tribes, and the son always had a desire to become a missionary physician. After graduating from the Kansas City Medical College and serving as an intern in the Kansas City Public Hospital, he went to Central Africa, where he lived for a number of years as the medical officer to an American mission. There he did considerable research in pure science, as well as in medicine, particularly in zoology and entomology. He published an elaborate monograph on the fevers found in Central Africa, as well as several articles on plants and a systematic, annotated check list of insects. He thus was brought

quickly into the scientific world and became well known in England and elsewhere as a student of entomology. Later, he went to California, where he taught at San Francisco, and ultimately to New Orleans.

Following that period of his life, he journeyed to Brazil, gave up the practice of medicine and became a mining engineer. He then turned to the field of literature, wrote novels and began to paint, changing his name to C. Kay-Scott. Thus he began a new career, in which he was eminently successful, for in addition to his painting, which was widely admired, he eventually became director of the Denver Art Museum and dean of the College of Fine Arts at the University of Denver. Ultimately, he was reunited with his family, from which he had been long separated. During his life he was married and divorced a number of times, but it was with the children of his first wife that he finally found himself happily reunited, looking back on an extraordinary career.

This autobiography is somewhat overwritten, but a physician will find much of interest in the book regarding an unusually talented man—physician, missionary, scientist, explorer, mining engineer, novelist and painter.

Internal Medicine in General Practice. By Robert P. McCombs, M.D. 8th, cloth, 694 pp., with 114 illustrations. Philadelphia: W. B. Saunders Company, 1943. \$7.00.

The author has written a classic type of practical textbook in an abbreviated form. He frankly states that he has had to appear dogmatic to achieve brevity, which lessens classroom value, but the book is well and entertainingly written, with more than a modicum of common sense through its pages.

The section on diagnosis follows orthodox lines. It is to be noted that the Hinton test is not included in the serologic tests for syphilis. The chapters on the heart, urinary tract and gastrointestinal tract are unusually complete for so small an edition, the last including a section on gastroscopy. The chapter on nutritional deficiencies is free from fantasy.

The blood dyscrasias are well covered. Infectious diseases are brought up to date, and there is an excellent chapter on the sulfonamide drugs, with an unusual listing of diseases in which the sulfonamides are not indicated. There is a brief note on penicillin. Chronic lung diseases and rheumatic disorders are ably discussed, and there is a chapter on the endocrine disorders. The field of allergy is briefly considered, and neurology and psychiatry are covered by a brief chapter on common neurologic and psychiatric problems.

The book is illustrated with excellent photographs, well-devised diagrams and a number of carefully selected x-ray plates.

The Nature and Treatment of Mental Disorders. By Dom Thomas Verner Moore, O.S.B., Ph.D., M.D. With a foreword by Edward A. Strecker, M.D. 8th, cloth, 312 pp. New York: Grune and Stratton, 1943. \$4.00.

Throughout this book the author maintains a benignly middle-of-the-road course that enables him, without crowding, jostling, or conflict, to salute Kraepelin, Freud, Jung, Adler, psychosomatics, neurology, statistics, commonsense and a number of other things and people of importance in psychiatry. Such benignity is especially becoming to the author as a member of the Order of Saint Benedict.

In his broad empiricism he includes his own psychiatric speculations and conclusions and a summary of investigative work that he himself has conducted and published earlier and elsewhere. Since the book is brief, his presentation of so many topics is certainly in some, and perhaps in most or all, of the cases necessarily superficial.

On the credit side his eclecticism enables him to display a wide range of psychiatric resources and methods—and, incidentally, he shows himself deft and resourceful in their utilization.

Throughout the book, general discussion is amplified by a large number of case histories. These are presented vividly and, as a rule, briefly; and in every case his analysis of therapeutic procedure is clear, and his estimate of therapeutic accomplishments is a model of honesty.

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STUDIES IN MEDICAL SOCIOLOGY

I. The Relation of Mental Disorders to the Community Socioeconomic Level

MAJOR ROBERT W. HYDE, M.C., A.U.S., AND SERGEANT LOWELL V. KINGSLEY, A.U.S.

BOSTON

THE purpose of this paper is to show the variations in incidence of mental disorders in the selectees from communities of different socioeconomic levels. No previous study of this type has been made of an unselected cross section of the male population.

Observations derived from rates of admission to mental hospitals have the obvious weakness of failing to eliminate the selective factor involved in hospitalization. They are not based on the examination of a cross section of supposedly normal persons, nor do they have the advantage of disclosing those mild, incipient, arrested or well-compensated disorders that in civil life may never lead to hospitalization. Even so, such studies have indicated that socioeconomic level may be influential in causing or precipitating mental disorders. Thus, Dayton,¹ in a study of admissions to hospitals for the insane in Massachusetts, showed that the most frequent mental disorders in the economically dependent group were mental deficiency and the senile and undiagnosed psychoses, whereas in the economically more fortunate group the involuntional psychoses and those due to drugs were more frequent; among illiterates mental deficiency and senile and alcoholic psychoses were most frequent, and in college men psychoses due to drugs, manic-depressive psychoses and psychopathic personalities were oftener seen. Such studies as Dayton's suggest the psychologic importance of the socioeconomic background.

METHOD OF STUDY

The area sending selectees to the Boston Armed Forces Induction Station is the eastern segment of Massachusetts within thirty-five miles of the seacoast. This area includes wealthy suburban communities, cities with active industries, poor industrial cities of low economic status, towns and villages of less than 2000 population and of varying

economic standards, some isolated rural communities and, finally, city slums in which all the distressing features of extreme poverty are to be found. Probably no more diversified social and economic strata could be found in any one area.

The community unit studied is the area under the jurisdiction of each local selective service board. This unit corresponds to a city ward, part of a small city, a large town or several neighboring small towns. Each community was evaluated and classified in terms of socioeconomic level (desirability). A community's desirability rating was arrived at after consideration of the following fundamental factors: medical care, educational facilities, recreational facilities, public works, "class,"* housing and welfare rates. This index is described elsewhere² in greater detail.

There are six classifications of community desirability; the best rating is A, the poorest F. Most of the communities with A ratings were suburban residential areas near enough to Boston to have the advantages of city life but far enough removed to avoid urban congestion. Most were beyond the 10-cent commuting limit, a significant boundary beyond which the city's poorer elements seldom move. Desirability B includes communities in the wealthier sections of Boston and the best neighborhoods in the other large cities. Desirability C and D represent a wide variety of middle-class communities in cities of all sizes and in some semirural areas. Most of the communities with E ratings were tenement areas in Boston and the other cities. Some of the communities included small slum areas. The F communities, or slum areas, were all in Boston, since it was considered that the worst Boston areas were in a class apart from even the slums of the smaller cities.

*"Class" includes an estimation of the general condition and appearance of houses, stores, factories and business buildings and the distance from the conveniences of a major city, and therefore an area's attractiveness as a residential section.

proach to the problem of occupational diseases as they occurred in the early nineteenth century in America. The essay was published in the *Transactions of the Medical Society of the State of New York*, and since only one hundred copies were printed, did not attract much attention and was not widely read. This reproduction of the text, with the scholarly introduction, is a valuable contribution to the history of the subject, and also to the history of medicine in the United States.

Functional Disorders of the Foot: Their diagnosis and treatment. By Frank D. Dickson, M.D., associate professor of clinical surgery, Medical School, University of Kansas, and orthopedic surgeon, St. Luke's, Kansas City General and Wheatley hospitals, Kansas City, Missouri, and Providence Hospital, Kansas City, Kansas; and Rex L. Diveley, M.D., colonel, M.C., A.U.S., and orthopedic surgeon, St. Luke's, Kansas City General, Research and Wheatley hospitals, Kansas City, Missouri, and Providence Hospital, Kansas City, Kansas. Second edition. 8°, cloth, 352 pp., with 202 illustrations. Philadelphia: J. B. Lippincott Company, 1944. \$5.00.

The second edition of this book, first published in 1939, has been completely revised and rewritten, and much new material has been added to the text. Two new chapters of timely interest have been inserted: one on functional disorders of the foot in relation to military service, and the other on foot disorders in relation to industry. The chapter on constitutional disease affecting the feet has been entirely rewritten.

The American Illustrated Medical Dictionary. By W. A. Newman Dorland, M.D., Lieutenant-Colonel, M.R.C., U.S.A., and member of the Committee on Nomenclature and Classification of Diseases, American Medical Association. With the collaboration of E.C.L. Miller, M.D., Medical College of Virginia. Twentieth edition. 8°, cloth, 1668 pp., with 885 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. \$7.50.

This new edition of an authoritative reference work has been completely revised with additions and alterations on every page. Many hundreds of new words have been included, particularly in the fields of biochemistry, chemotherapy, allergy, endocrinology, vitamin research, tropical and parasitic diseases and mycology. Special attention has been devoted to the vocabulary of war medicine and surgery, as well as to the great number of new synthetic drugs and medical preparations. The terminology of this new edition has been made to conform with the "Standard Nomenclature of Diseases and Operations" of the American Medical Association. This dictionary is remarkable for its system of condensation, resulting in the production of a volume of handy size.

A Manual of Physical Therapy. By Richard Kovács, M.D., professor of physical therapy, New York Polyclinic Medical School and Hospital, attending physical therapist, Manhattan State, Harlem Valley State, Columbus and West Side hospitals, visiting physical therapist, New York City Department of Correction Hospitals, consulting physical therapist, New York Infirmary for Women and Children, and Mary Immaculate Hospital, Jamaica, New York, St. Charles Hospital, Jefferson, Long Island, and Hackensack Hospital, Hackensack, New Jersey. Third edition. 12°, cloth, 309 pp., with 118 illustrations. Philadelphia: Lea and Febiger, 1944. \$3.25.

This small manual, originally entitled *Physical Therapy for Nurses*, was renamed after it had been written, amplified and brought up to date to furnish a comprehensive volume from the viewpoint of wartime and postwar physical therapy. It is intended as an aid in elementary training on the subject, as well as a manual for physicians and medical personnel seeking information on physical therapy. The plan of the manual is to proceed from a brief statement of the basis and the evolution of physical therapy to a systematic presentation of the physics, physical and physiologic effects, clinical uses, technic of application, and dangers and contraindications of each of the principal physical treatment methods. The text is divided into the headings of heat and light, electricity, water, and massage and exercise. The last two chapters have to do with physical therapy in institutional practice and physical therapy in war.

Manual of Human Protozoa: With special reference to their detection and identification. By Richard R. Kudo, D.S., associate professor of zoology, University of Illinois. 11° cloth, 125 pp., with 29 illustrations. Springfield, Ill.: Charles C Thomas, 1944. \$2.00.

This small manual is designed for class use and is based on the author's laboratory notes that have been used in teaching at the University of Illinois. It is intended as a supplement to the large treatises on protozoology. The book contains essential information needed as a practical guide in detecting and identifying the human protozoa. A number of original drawings prepared from living specimens and microscopic preparations have been inserted in the text to supplement the descriptions of the various types of protozoa. This small manual should be of service to all those interested in elementary knowledge of human protozoa.

Freedom from Fear: The interrelation of domestic and international programs. By Louis H. Pink, president of Associated Hospital Service of New York. With a foreword by Owen Young. 8°, cloth, 254 pp. New York and London: Harcourt and Brothers, 1944. \$2.50.

The aim of this small book is to emphasize the importance of domestic measures for social security and to show that these measures are inadequate unless they are supplemented by broad, economic security and universal prosperity. Approximately half the text is devoted to the discussion of various forms of insurance. The book also includes sections on hospitalization, industrial medicine and the cost of medical care, all of which may be of interest to physicians.

NOTICES

SOUTH END MEDICAL CLUB

The eighteenth year of the South End Medical Club will begin on Tuesday, October 17, at 12 noon, at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

Dr. Henry Baker, clinical professor of medicine, Tufts College Medical School, will speak on the subject "Stern Puncture Therapy."

Physicians are cordially invited to attend.

ANNOUNCEMENT

Dr. C. A. Cheever announces a change of address: from 464 Beacon Street, Boston, to the Alexander Home, 29 Fir Parish Road, Scituate, Massachusetts.

INTERNSHIPS AND RESIDENCIES AT ST. ELIZABETHS

The Civil Service Commission announces a new examination for rotating internships and psychiatric residencies at St. Elizabeths Hospital, the federal institution for the treatment of mental disorders, in Washington, D. C. The positions pay \$2433 a year, including overtime pay.

The internships consist of nine months of rotating service including medicine, surgery, pediatrics (affiliation), obstetrics (affiliation) and, as conditions permit, psychiatry and laboratory. Applicants must be third-year or fourth-year students in an approved medical school.

The psychiatric residencies consist of nine months in psychiatry. Applicants must have successfully completed the fourth year of study in a medical school and they must have the degree of B.M. or M.D. In addition they must have completed an accredited rotating internship of at least nine months or be serving such internship at the time of making application. Persons who attain eligibility but who are still serving their internship may have their names submitted for appointment but they cannot enter on duty until they have completed their internship.

There are no age limits for this examination and no written test will be given. Applications will be accepted until the needs of the service have been met. Application forms may be secured at first- and second-class post offices, from the commission's regional offices, or direct from the United States Civil Service Commission, Washington 25, D. C.

(Notices continued on page xxi)

signed to measure the subject's ability to learn. though these tests are devised so as to minimize language handicaps, these and cultural handicaps probably affect the test results.

Table 2 shows a steplike increase in the rates of mental deficiency with a decline of socioeconomic level in the community, from 0.9 per cent in the best communities to 3.0 per cent in the poorest. The correlation is further supported by the fact that the average desirability rating for the 11 communities with the highest rates for mental deficiency was above E. In addition, 4 of the 11 were F desirability, in contrast to the fact that 6 of

TABLE 2. *Relation of Percentage Rejected for Mental Deficiency to Community Socioeconomic Level.*

SOCIOECONOMIC LEVEL	PERCENTAGE REJECTED
A	0.9
B	1.0
C	1.4
D	1.5
E	2.3
F	3.0

of the 11 with the lowest rates were of A or B desirability.

The finding of high rates of mental deficiency in the lowest socioeconomic group is consistent with the finding of Dayton¹ that psychosis with mental deficiency is the most frequent disorder in the economically dependent group.

The high incidence of mental deficiency in the lower socioeconomic levels can be only partially explained on the basis either of the increased proportions of immigrant families with their language and cultural handicaps or of the biologic differences that have been attributed to them. The explanation does not appear to be complete. It is expected that those who are handicapped by defective intelligence and who fail in the economic competition of society will gravitate into the more undesirable areas, whereas those having the most ability will progress to desirable communities. Furthermore, with inheritance of mental deficiency there tends to be an additional increase of mental deficiency in the poorer communities into which the most defective gravitate or from which they fail to rise.

The explanation of Faris and Dunham³ appears to be extremely pertinent. They say:

Normal mentality and behavior develops over a long period of successful interaction between the person and these organized agencies of society. Defects in mentality and behavior may result from serious gaps in any part of the process. The failure of society to transmit language, for example, or even partial failure through parental neglect of children results in mental retardation of the children.

Psychopathic Personality

Psychopathic personalities, as described in *Mobilization Regulations*,⁶ are an ill-defined group of persons who "manifest a definite defect in their ability to profit by experience . . . [and] are unable to

respond in an adult social manner to the demands of honesty, truthfulness, decency and consideration of their fellow associates." In this group are those who do not conform in their conduct to the dictates of society as a whole or who, by reason of repeated acquisitive, sexual, pugnacious or statutory offenses, together with poor work records and irresponsibility, are considered to be too great trouble-makers to be of use in the Service.

The greatest variation in rejections for psychopathic personality as shown in Table 3 are at the extremes of socioeconomic level. Throughout the intermediate socioeconomic levels, B, C, D and E, there is little variation in the rate for psychopathic personality.

It is notable that of the 15 communities with the extremely high rates, 7 were of the lowest desirability (F) and of population density of over 20,000. Of the 15 communities with extremely low rates, 7 were of A or B desirability and no Boston communities or those of population density over 10,000 are represented.

The explanation of the relation of psychopathic personality to socioeconomic level is not clear, for it is difficult to separate cause and effect. On the one hand, it is known that the psychopath tends to gravitate into the undesirable community; on the other hand, it appears that the stresses and needs

TABLE 3. *Relation of Percentage Rejected for Psychopathic Personality to Community Socioeconomic Level.*

SOCIOECONOMIC LEVEL	PERCENTAGE REJECTED
A	2.4
B	3.3
C	3.1
D	3.6
E	3.9
F	6.9

that arise at the low economic levels tend to provoke reactions that are predominantly psychopathic rather than neurotic.

The direct effect of poverty appears to be important. As Burton⁷ stated, "We will turn parasites and slaves, prostitute ourselves, swear and lie, damn our bodies and souls, forsake God, abjure religion, steal, rob, murder rather than endure this insufferable yoke of poverty, which doth so tyrannize, crucify and generally depress us." The natural reaction to the physical stress of poverty appears to be one of anger and acquisitiveness. One reason for the great increase in the rate for psychopathic personality in the F communities over that in the E communities may be that it is only in the former that the real oppression of poverty exists to any marked degree.

It is to be noted that the poorest communities are also the most crowded, and that they contain the highest proportion of foreign-born population or native-born of foreign parents. It is impossible to determine the relative importance of specific immi-

The 60,000 men investigated in the course of this study were examined during the winter, spring and summer months of 1941-1942. The age limits of the first 6000 men were twenty-one to thirty-four, and those of the remainder twenty-one to forty-four years, both inclusive. They were all examined by the same team of psychiatric examiners, using the same criteria for diagnosis. Most of the selectees were unmarried, and no fathers with children born before Pearl Harbor were included.

In determining the relation of mental disorders to socioeconomic level, the percentage of selectees rejected for each disorder from each community was determined, and from this the average rate for communities of like socioeconomic level was calculated. This was done for mental deficiency, psychopathic personality, chronic alcoholism, psychoneurosis, psychoses and the total of these five disorders. Miscellaneous disorders that fell into none of these categories were not studied.

It is recognized that no hasty generalization can be made from the single correlation of mental disorders with desirability. False conclusions may be reached if such major factors as the percentage of foreign-born and natives of foreign-born parents and the density of population are not isolated and their significance considered. It would be an error to attempt to explain our findings without the consideration of both biologic and cultural factors. The emphasis of this paper, however, is only on the cultural factors that exist in the communities studied and are more easily recognized than are the biologic factors. There is no intention of slighting the significance of the latter.

As a working hypothesis it is assumed that the biologic factors of importance in mental disorders interact with environmental factors, the influence of which is such that the prevalence of mental disorders within a community varies with the amount of mental stress and with the availability of the normal emotional outlets of recreation, religion, home life and work. The types of mental disorders vary both with the type of mental stress and with the cultural acceptability of different emotional outlets.

RESULTS

The relation of desirability to the total of the major causes of psychiatric rejection is presented in Table 1. It shows a steplike increase in the proportion of selectees disqualified for the major rejection causes from the best to the worst communities.

A comparison between the communities with extremely high rejection rates and those with extremely low rates yields the following results: In 13 communities with the highest rejection rates, the average desirability rating was E, there were 7 F communities (only 9 communities in the entire area were given F ratings), and 8 communities were in Boston. In thirteen communities with the lowest rates, the average desirability rating was B, not a

single community was in Boston, 9 communities were suburbs of Boston, and no community was in the lower half of the desirability scale (D, E or F).

The finding of an increased rate of psychiatric disorders in the poorest communities suggests that the low socioeconomic level may be of etiologic im-

TABLE 1. *Relation of Total Major Psychiatric Causes of Rejection to Community Socioeconomic Level.*

SOCIOECONOMIC LEVEL	APPROXIMATE NO. EXAMINED	PERCENTAGE REJECTED
A	6,250	7.3
B	6,450	9.2
C	16,900	9.4
D	15,000	10.0
E	8,650	12.7
F	6,750	16.6

portance. The finding is in agreement with that of Faris and Dunham,³ who found that the highest admission rates for mental disorders occurred in the poorest areas of the city (Chicago). This condition may be the result of several factors. The importance of socioeconomic level is further demonstrated in the consideration of communities of the same population density. It was notable that 12 of the 14 communities that had unusually low rates for mental disorders were of a higher socioeconomic level than the average for the density level in which they were classified.

Certain factors that must be considered to affect the relation of mental disorders to socioeconomic level are those of difference in population density, in proportions of people of foreign birth, and in nationality, which are associated more closely with certain socioeconomic levels than with others. The fact that people with special physical and mental handicaps gravitate into the communities of the lowest socioeconomic level and also fail to rise from such communities to better ones is of acknowledged importance. In general, however, a great part of the findings must be attributed to the true influence of the different socioeconomic levels rather than to the influences of these interrelated factors. The respective influence of population density and of nationality will be considered in subsequent papers.^{4, 5}

Since each mental disorder appears to bear a different relation to socioeconomic level, as has been suggested by the work of Dayton¹ and that of Faris and Dunham,³ the major psychiatric rejection causes are considered separately.

Mental Deficiency

To state exactly the minimum intelligence standards except in terms of the score on the tests used would be difficult, but it may be said that in general the test procedure was designed to disqualify men whose mental age was estimated to be below ten years.

Mental ability is determined by a team of psychologists, using a series of psychometric tests

ie explanation for this, according to Gillespie,⁹ is pressed in the maxim, "He that is down need fear fall."

The distribution of different nationalities at different socioeconomic levels may be important, for the studies of mental disorders and nationalities great variation in rate of psychoneurosis was found. Whereas mental deficiency, psychopathic personality and chronic alcoholism are all associated with economic and social failure, thus preventing the subject from climbing the socioeconomic ladder, the reverse is true in the majority of the cases of psychoneurosis. The neurosis may be part of their drive or ambition. It may be either the cause or the result of ascent of the social or economic ladder. The subject can be severely neurotic and still be extremely successful. Hence, if there is any inheritance of a neurotic disposition, persons with this inheritance would be likelier to reach higher socioeconomic levels than would be those inheriting biologic limitations of intelligence.

Beard¹⁰ was perhaps correct when he postulated that America is a nation of neurasthenics, and that the condition is fostered by American ambition and is therefore most prevalent in the great American middle classes. Other explanations are found, first in the difference in the types of stress to which those at the various socioeconomic levels are subjected; and secondly, in the differences in acceptability of emotional outlets in communities of varying culture.

When the needs of persons in the desirable communities, which are usually intellectual, are frustrated and stress ensues, they are less apt to behave in the asocial manner of the psychopath than are those in the slums when their needs, which are usually more elementary or physical, are frustrated. Furthermore, the asocial behavior of the psychopath is not acceptable at the upper social levels, since the members of the most desirable communities are more restrained by the laws and customs of society. The boy in the gang in the slums reacts to stress by surpassing the gang in whatever exploits of drinking, fighting, car-stealing or girl-chasing it is engaged in; the boy in the better community reacts to his less elementary type of frustration by means of nervous indigestion, headaches and anxiety. Hence, chronic alcoholism and psychopathy are found in the poorer communities and psychoneurosis in the more desirable ones.

Biologic explanations cannot be ignored. Presumably some people are constitutionally predisposed either to psychopathy or to neurosis. The true picture is probably one of the interplay of different cultures on different predispositions. What is important at this point is the clear distinction between psychoneurosis and psychopathy in their occurrence in the communities of various socioeconomic levels.

Psychoses

Because those hospitalized for mental disorders, as well as many with histories of such hospitalization, are not being submitted for examination, data on the psychoses are not representative of the true incidence of psychoses in the population. Consequently, far less importance can be attached to our findings in this particular realm of psychiatric disorders. The data seem worthy of presentation, however, for they do represent psychotic cases in the general population in the area studied.

Table 6 shows a definite increase in incidence of psychoses in the poorer socioeconomic levels over that in the best communities, with the communities of intermediate desirability, B to E, having intermediate rates not significantly different from each

TABLE 6. *Relation of Percentage Rejected for Psychosis to Community Socioeconomic Level.*

COMMUNITY SOCIOECONOMIC LEVEL	PERCENTAGE REJECTED
A	0.16
B	0.36
C	0.28
D	0.41
E	0.36
F	0.45

other. This pattern most closely resembles that of psychopathic personality and does not resemble that of psychoneuroses. The findings correspond roughly to those of Faris and Dunham³ in their report on institutionalized psychotic patients in Chicago.

The gravitation of the inadequate to the lower socioeconomic level must be considered as an important factor, for the psychoses, like all mental disorders except psychoneurosis, are conditions that are socially and economically handicapping to such an extent that they prevent their victims from rising to a higher socioeconomic level. In so far as inheritance is a factor in producing a predisposition toward mental disorders, it might be expected that the influence of inheritance would be greatest in communities where there are the largest number of persons with mental disorders — in this case, in the communities of lower desirability. It is probable that withdrawal as a result of submission to the stress of life, a symptom seen in dementia praecox, the most frequent psychosis in the selectee age group, is most frequent at the lowest socioeconomic level. In explaining the incidence of psychoses it is probably necessary to consider both biologic and cultural factors. To do so requires study of the true proportion of psychotic persons to be found in society, either institutionalized or otherwise, a project beyond the scope of this study.

grant stresses and cultural differences among people of foreign origin as factors in the increase of psychopathy. It might be pointed out, however, that no one nationality is especially prevalent in the undesirable communities. Mediterranean groups, Irish, Canadians, Negroes and Old Americans are all well represented. It can be inferred that causal factors are not associated with any one race, but are associated with any national group that inhabits the undesirable community, a fact that Shaw⁸ emphasized.

Chronic Alcoholism

According to *Mobilization Regulations*,⁶ the criterion of disqualification for chronic alcoholism is defined as follows: "An individual will be regarded as a chronic alcoholic if he habitually uses alcohol to a point of social or physical disability, as evidenced by loss of job, repeated arrests, or hospital treatment because of alcoholism." As shown by Table 4, there is no significant variation in the per-

TABLE 4. Relation of Percentage Rejected for Chronic Alcoholism to Community Socioeconomic Level.

SOCIOECONOMIC LEVEL	PERCENTAGE REJECTED
A	1.0
B	0.9
C	0.9
D	1.2
E	1.5
F	2.8

centage rejected for chronic alcoholism throughout the most desirable half of the communities, with a variation only from 0.9 to 1.2 per cent in the levels A through D.

The fact that the rates of alcoholism bear no relation to socioeconomic level in the higher brackets suggests that other factors correlate more closely with alcoholism. The greater population density in the communities of D, E and F desirability may account, at least in part, for the increase in chronic alcoholism in those communities. In general, within a given socioeconomic level there is found a tendency for alcoholism to increase in the denser communities.

It may appear significant that the 11 communities with extremely high rates for alcoholism had an average desirability of E, as compared to the average of less than C for the 11 communities with extremely low rates. The 6 F-desirability communities that had extremely high rates, however, were also of the highest population density, over 20,000, suggesting that density may be the primary factor.

On the whole, heavy drinking and drunkenness are less taboo in the poor, low socioeconomic communities than throughout the upper and middle desirability brackets. Heavy drinking as an emotional outlet and as a form of social and physical relaxation is acceptable in the culture of the labor-

ing classes, who make up the lowest desirability brackets. The tavern is the poor man's club, and when he "accidentally" overindulges and become drunk, he has committed no great moral or social transgression; he has suffered no such loss of social prestige as might occur in the higher social strata. With greater cultural acceptability of hard drinking and drunkenness, it is not surprising that alcoholism is increased in the poorer communities. With the use of alcohol as an outlet for emotional stress and for physical relaxation, outlets such as neurosis are less necessary, as is apparent in the next consideration.

Psychoneurosis

A well-defined psychoneurosis of any type is considered disqualifying for military service. Some of the symptoms and types are designated in *Mobilization Regulations*⁶ as conversion symptoms, hysterical paralysis, vasomotor disturbances, excessive concern over minor or imaginary bodily ailments, obsessions, compulsions, phobic manifestations and emotional disturbances.

The relation of psychoneurosis to community socioeconomic level (Table 5) differs from that of the mental disorders previously considered in that there is no significant increase in psychoneurosis with decreased socioeconomic level. There is no appreciable rise when communities of extremely high rates are compared with those that have low rates. Ten communities with the highest rates for psychoneurosis had an average desirability rating of D and those with the lowest rates a rating of C. This is

TABLE 5. Relation of Percentage Rejected for Psychoneurosis to Community Socioeconomic Level.

SOCIOECONOMIC LEVEL	PERCENTAGE REJECTED
A	2.9
B	3.7
C	3.8
D	3.4
E	4.7
F	3.4

the smallest comparative difference observed in any of the mental disorders.

In 8 of the 10 communities with extremely high rates, the desirability rating was either C or D. On the other hand, 6 of the 10 communities with extremely low rates were also in the C or D brackets. These findings suggest that there is little or no relation between psychoneurosis and socioeconomic level.

The relatively low rates of psychoneurosis in the poorer communities confirm the findings of Newstatter.⁹ His study showed that nervousness of nearly all kinds was actually less frequent among children of the poor than among children of the well-to-do. Twenty per cent of the children of the poorer families and 38 per cent of those of the well-to-do parents had nervous or neurotic symptoms.

The explanation for this, according to Gillespie,⁹ is expressed in the maxim, "He that is down need fear no fall."

The distribution of different nationalities at different socioeconomic levels may be important, for in the studies of mental disorders and nationalities a great variation in rate of psychoneurosis was found.

Whereas mental deficiency, psychopathic personality and chronic alcoholism are all associated with economic and social failure, thus preventing the subject from climbing the socioeconomic ladder, the reverse is true in the majority of the cases of psychoneurosis. The neurosis may be part of their drive or ambition. It may be either the cause or the result of ascent of the social or economic ladder. The subject can be severely neurotic and still be extremely successful. Hence, if there is any inheritance of a neurotic disposition, persons with this inheritance would be likelier to reach higher socioeconomic levels than would be those inheriting biologic limitations of intelligence.

Beard¹⁰ was perhaps correct when he postulated that America is a nation of neurasthenics, and that the condition is fostered by American ambition and is therefore most prevalent in the great American middle classes. Other explanations are found, first in the difference in the types of stress to which those at the various socioeconomic levels are subjected; and secondly, in the differences in acceptability of emotional outlets in communities of varying culture.

When the needs of persons in the desirable communities, which are usually intellectual, are frustrated and stress ensues, they are less apt to behave in the asocial manner of the psychopath than are those in the slums when their needs, which are usually more elementary or physical, are frustrated. Furthermore, the asocial behavior of the psychopath is not acceptable at the upper social levels, since the members of the most desirable communities are more restrained by the laws and customs of society. The boy in the gang in the slums reacts to stress by surpassing the gang in whatever exploits of drinking, fighting, car-stealing or girl-chasing it is engaged in; the boy in the better community reacts to his less elementary type of frustration by means of nervous indigestion, headaches and anxiety. Hence, chronic alcoholism and psychopathy are found in the poorer communities and psychoneurosis in the more desirable ones.

Biologic explanations cannot be ignored. Presumably some people are constitutionally predisposed either to psychopathy or to neurosis. The true picture is probably one of the interplay of different cultures on different predispositions. What is important at this point is the clear distinction between psychoneurosis and psychopathy in their occurrence in the communities of various socioeconomic levels.

Psychoses

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The gravitation of the inadequate to the lower socioeconomic level must be considered as an important factor, for the psychoses, like all mental disorders except psychoneurosis, are conditions that are socially and economically handicapping to such an extent that they prevent their victims from rising to a higher socioeconomic level. In so far as inheritance is a factor in producing a predisposition toward mental disorders, it might be expected that the influence of inheritance would be greatest in communities where there are the largest number of persons with mental disorders—in this case, in the communities of lower desirability. It is probable that withdrawal as a result of submission to the stress of life, a symptom seen in dementia praecox, the most frequent psychosis in the selectee age group, is most frequent at the lowest socioeconomic level. In explaining the incidence of psychoses it is probably necessary to consider both biologic and cultural factors. To do so requires study of the true proportion of psychotic persons to be found in society, either institutionalized or otherwise, a project beyond the scope of this study.

COMMENT

Relations have been established between community socioeconomic level and the total rate of major mental disorders and between each of the major mental disorders. That the relations thus established are not the same for all disorders is in agreement with the findings of Faris and Dunham³ in their study of hospital admissions from different areas of Chicago. It is significant that a study of disorders severe enough to require hospitalization and a study of disorders among supposedly normal selectees examined for induction into the armed forces should reach similar conclusions. The findings of this study suggest that those of Faris and Dunham represent the true conditions and cannot be attributed to the selective factor involved in hospitalization.

Various explanations of the causes of the relation of mental disorders to community socioeconomic level have been offered, not because these explanations are considered final and capable of proof, but to stimulate further research. Intensive study of the interrelation of biologic and environmental factors in mental disorders is essential.

Further differentiation of disease entities and variation in symptomatology due to the cultural differences is necessary to explain such findings as higher rates for psychoneurosis in the best communities and for psychopathic personality in the poorest.

The influence of the mobility of the unfit in their gravitation into the undesirable areas must be evaluated. The influence of both biologic differences in the foreign-born and their children and their specific cultural differences and handicaps must be isolated. The interrelation of socioeconomic level, nationalities and occupation with population density must be found.

An attempt will be made in two subsequent papers^{4, 5} to present the relation of mental disorders to population density and to race and nationality, but these papers likewise point out the immensity of the field yet to be investigated.

SUMMARY

The rejection rates for the major causes of mental rejections in 60,000 selectees examined at the Boston Armed Forces Induction Station were determined and classified according to the socioeconomic level of the community from which the selectees came. An attempt was made to show the relation of mental disorders to socioeconomic factors.

The total incidence of major mental disorders increased gradually from 7.3 per cent in the best communities to 16.6 per cent in the poorest communities.

There was a steplike increase in the rate of mental deficiency as socioeconomic level of the community declined, from 0.9 per cent in the best communities to 3.0 per cent in the poorest.

The rate of psychopathic personality increased from 2.4 per cent in the best communities to 6.9 per cent in the poorest. In spite of the wide difference at the extremes there was little variation among communities of intermediate desirability levels.

The rate for chronic alcoholism did not vary significantly in the better half of the communities (A, B and C desirability) and increased only in the poorest and densest (D, E and F) communities, suggesting that socioeconomic level per se is secondary in importance to density of population in determining the incidence of chronic alcoholism.

The rate for psychoneurosis showed no consistent variation with socioeconomic level. There was no increase in the poorer communities, whereas throughout the communities of intermediate desirability there was a slight increase.

The rate of psychoses increased with declining socioeconomic level, and variation from the average was most marked at the two extremes of desirability.

These findings were explained on the basis of gravitation of the more unfit into the poorer communities and of differences in cultural acceptability of asocial conduct at different socioeconomic levels. Exceptions due to population density and nationality were considered and will be presented in full in subsequent papers.

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UTERINE BLEEDING AND THE ROENTGENOLOGIST*

JOE VINCENT MEIGS, M.D.†

BOSTON

ABNORMAL uterine bleeding is perhaps the most frequent abnormality of the menstrual cycle. The causes of such bleeding are many, and before proper treatment can be instituted consideration should be given to the various physiologic changes that may be responsible. It is not sufficient to do a dilatation and curettage, give the patient radium or x-ray treatment or remove the uterus, for correction may be by way of some endocrine preparation or vitamin or even something as remote from pelvic attack as splenectomy. One of the greatest mistakes that can be made is to treat bleeding patients without proper investigation; surely, before x-rays are directed toward the ovaries the reason for the bleeding must be as clear as possible. Patients with scurvy or purpura should not be given x-ray treatment, and its use to check bleeding that may be due to cancer of the fallopian tube or endometrium is to be condemned. In the presentation of this subject a review of the various changes that may be responsible for abnormal bleeding is considered first, with a discussion of the means at one's disposal to correct such abnormalities. Lastly, the various methods of surgical and radiologic attack are discussed.

TYPES OF ABNORMAL BLEEDING

Physiologic Disturbances

The first consideration should be given to a description of the constitution of menstrual blood. Is it different from normal blood? Does it contain an anticoagulant or a toxic product, or can normal physiology explain its characteristics? In 1942 Lozner, Taylor, and Taylor¹ presented a well-thought-out and well-controlled series of experiments that showed that menstrual blood and defibrinated blood or serum react similarly to the addition of thrombin, prothrombin and fibrinogen. Their experiments demonstrated that menstrual blood is blood that has already clotted within the uterine cavity. They explain the lack of clots as seen in the menstrual flow as due to the fact that menstrual blood is slowly excreted, and they believe that there may be some lytic substance within the uterine cavity. In most patients small clots are usually found, and having taken histories for many years from patients on this point, I can agree. The experimenters showed that when prothrombin or fibrinogen was added to menstrual blood, clotting occurred. They indicate that menstrual blood has sufficient clot-promoting activity

to clot if prothrombin and fibrinogen are added to it. This reaction to prothrombin and fibrinogen is similar to that of defibrinated blood or serum. Their work demonstrates that menstrual blood as passed from the vagina consists of serum, clots and debris, and that clotting should take place before the menstrual fluid reaches the vagina. It is obvious, therefore, that any interference with the normal structure of the uterus or of the normal constituents of the blood may be a cause of abnormal bleeding.

Another primary consideration is an understanding of the coagulation of blood. It is usually accepted that blood clots because calcium, prothrombin and blood platelets act together to form thrombin, an active coagulant. Thrombin with fibrinogen forms fibrin, the basis of the blood clot so that interference with any of the above constituents of blood may prevent clotting and hence cause abnormal menstrual flow. Lozner, Taylor and Taylor have explained that coagulation nearly always takes place within the uterus. If, for instance, the blood platelets are few or absent, thrombocytopenic purpura results. A deficiency of calcium may be a cause of abnormal bleeding. Certainly a deficiency of prothrombin is a cause, and such abnormal bleeding may easily occur during the phase of uterine bleeding. There are possibilities for bleeding in any changes that occur in the physiologic characteristics of blood.

Certain of the blood dyscrasias, such as thrombocytopenic purpura, are definitely associated with abnormal uterine bleeding, and nearly every year a case of bleeding requiring splenectomy, not hysterectomy, is seen in the wards of the hospital. Certainly some of the leukemias evidence uterine bleeding as a symptom. There are other abnormalities of the cellular blood elements that may be responsible for bleeding.

Before consideration can be given to hormones as being responsible for abnormal bleeding, or before sympathetic-nerve control of uterine blood vessels can be discussed, the present conception of menstruation must be explained. Normal menstruation recurs cyclically — why, no one knows. It occurs normally only during certain years in the lives of women. Before and after these normal years any uterine flow must be considered as abnormal until proved otherwise. Normal menstruation occurs after a follicle, secreting estrin, has grown and ruptured and a corpus luteum, secreting progesterin, has grown and retrogressed. It occurs when both estrin and progesterin are low in amount. Markee² has pointed out that before the time of menstruation the edema of the premenstrual phase lessens and the endometrium becomes thinner. At

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†Chief of the Vincent Memorial Hospital at the Massachusetts General Hospital; clinical professor of gynecology, Harvard Medical School.

the same time the veins of the endometrium are swollen and congested and the return flow of blood from the endometrium is delayed. This is due to a constriction of the smooth muscle of the uterus. Some of the veins rupture, some leak blood by rhexis, and hematomas are found lifting up the endometrium. Later, owing perhaps to a direct hormonal influence or to sympathetic control, the spiral arteries become shut off. Anoxemia then occurs, sloughing commences, and the endometrium is cast off. The open spiral arterioles present into the uterine cavity. Later these arteries relax, a few at a time, and bleeding takes place from them into the uterine cavity. This is a rhythmic process, and because only a few spiral arteries bleed at a time, severe hemorrhage does not take place. The basal layer of the endometrium with its straight arteries is not injured, and because of this, repair takes place and the endometrium covers the raw surface and bleeding ceases. Ovarian hormones are responsible for some of this effect, but whether the effect is on the muscles of the uterus or the walls of the veins and arteries or their nerve apparatus is unknown. It is reasonable to assume that some of the activities of the blood vessels are due to the influence of the sympathetic nervous system and its mediator, sympathin (adrenaline). There is definite evidence of a hormonal control, for without hormones, as in the menopause, normal uterine bleeding does not occur.

There has long been a theory that the initiation of menstrual bleeding is due to the lowering of the titer of estrin. In the castrated patient, cessation of estrin treatment is often followed by bleeding. If, however, estrin and progestin are given together, withdrawal of estrin is not followed by bleeding but withdrawal of progestin is. Thus, bleeding can be precipitated by the withdrawal of either hormone.

A definite type of bleeding is seen in those patients who do not ovulate. In this group, bleeding may be fairly regular and yet a normal cycle is not present, for progestin is absent. Ovulation does not occur in the cases of abnormal bleeding oftenest seen, that is, those of metropathia hemorrhagica.

Control by the sympathetic nervous system must be a factor in some cases, for section of the spinal cord often precipitates bleeding. It is well known that within three days after presacral neurectomy, no matter what the time of the cycle, bleeding nearly always occurs. Anger and fright are well known as precipitators of menstrual cycles. It is quite possible that hormones and nerve control go hand in hand and that one affects the other. It is certain, however, that the former are the more essential of the two, for without them physiological bleeding does not occur.

Hormonal Dysfunction

The most frequent hormonal pattern of abnormal bleeding is that so often seen in early and late menstrual life. This type of bleeding has been called metropathia hemorrhagica; it is characterized by hyperplasia of the endometrium, a sizable follicle cyst of the ovary, wrinkling of the rest of the ovarian tissue and the absence of corpus luteum. The history is usually fairly typical — an occurrence of normal or large periods followed by continuous flowing or, as is most usual, a period of amenorrhea followed by prolonged flowing. Young patients are not usually operated on, but in certain ones that have been such an ovarian picture has been encountered. In patients in the menopause group when the ovaries are ceasing to function it is not at all uncommon. The treatment should be simple — the institution of a corpus luteum-stimulating hormone or substitution of corpus luteum itself. Since there is no satisfactory corpus luteum-stimulating hormone, progestin or the corpus-luteum hormone is frequently used and with good effect. This hormone is given on successive days, and after its withdrawal a normal period occurs from a secretory endometrium. After three successive cycles the treatment is stopped, and in about 50 per cent of cases a normal cyclic rhythm is established. This group of patients may also be treated by large doses of estrin or of testosterone with about the same results.

Other cases of bleeding, such as those resulting from a secretory endometrium, are not so clearly understood, and it is possible that they fall into another group. In certain cases, young patients have large, white ovaries through which ovulation cannot take place. They usually have amenorrhea but may complain of continuous bleeding. This bleeding is due to the persistent secretion of small amounts of estrin. Transecting or peeling the ovary in such a way as to allow ovulation to take place usually relieves the situation. The hormone that is the ordinary cause of bleeding is estrin; it is usually present in small but persistent amounts and is not interrupted by ovulation. Bleeding due to hyperplasia of the endometrium is the same sort of phenomenon.

Included under hormonal causes of bleeding from the uterus are the various tumors of the ovary that secrete estrin and therefore cause the estrin type of bleeding or the type that is found in the anovulatory cycle. Granulosa-cell tumors, thecomas and certainly many ovarian cysts that secrete estrin cause such bleeding. This bleeding comes from an estrin-phase endometrium. It is obvious, then, that the real cause of hormonal bleeding is the uninterrupted production of estrin, usually of a small but persistent amount.

Vitamin Deficiencies

Next to be considered is the bleeding due to vitamin deficiencies. The most obvious type is that due to vitamin C deficiency, or scurvy. In scurvy, continuous bleeding may be slight, severe or prolonged. The cure is to replenish the body with vitamin C. Prothrombin deficiency due to liver injury may be a cause of abnormal bleeding, and a prothrombin deficiency due to lack of vitamin K, either because of lack of it or because of injury to the bile-salt supply, does the same thing. Biskind and Biskind³ have recently found that perfect conjugation of estrogen in the liver may be impossible without sufficient vitamin B, and it is possible that such a deficiency is responsible for abnormal bleeding from the uterus.

Nerve Factors

The central nervous system probably plays no part in the control of the bleeding, but the sympathetic system, with its action on the blood vessels through its mediator sympathin (adrenaline), must and does affect bleeding. As described above, injury to the spine or injury by surgery to the superior hypogastric plexus brings about sudden bleeding.

Pathologic Lesions

Certain lesions may in themselves be the cause of bleeding because of changes in the shape of the uterine cavity, because of interference with the normal blood-vessel control or because bleeding may occur directly from a broken blood vessel, as in a tumor.

A *polyp of the cervix* bleeds because of trauma to its surface or lack of blood supply to its tip and subsequent necrosis. A *polyp of the endometrium* bleeds because of interference with its blood supply or that of the endometrium, which it abuts, or because of interference with the normal contraction of the uterus and closure of its cavity. *Leiomyomas* or *fibroids* are responsible for bleeding because of interference with the normal contracting mechanism of the uterine wall or with the blood vessels of the endometrium, or because, as in submucous fibroids, they present a greatly increased bleeding surface. It is possible that because of their position they interfere with the endometrial blood supply, whether they are submucous or intramural. Any lesion that increases the surface of the endometrial cavity causes abnormal bleeding, for the amount of blood lost from an increased surface cannot clot and disintegrate within the uterus — hence the occurrence of bright bleeding and clots. In a large number of cases, however, fibroids bleed because there is an accompanying endocrine disturbance. This dis-

turbance is always that of anovulation, and anovulation is responsible for the type of bleeding seen in metropathia hemorrhagica. Patients with *pelvic inflammation* bleed because the ovaries, buried in adhesions, cannot ovulate and a follicle cyst is formed that secretes estrin. No ovulation occurs, and metropathia hemorrhagica therefore exists. *Ovarian cysts* cause bleeding because they often secrete low but persistent amounts of estrin and produce an estrin-phase endometrium that eventually bleeds. *Cancer of the cervix* bleeds because pieces of cancer become necrotic and break off, and because the tumor itself is sometimes traumatized. *Cancer of the endometrium* bleeds because pieces of tumor become necrotic and because constriction of the uterus injures the delicate tumor mass. Patients with *cancer of the fallopian tube* bleed because pieces of tumor often slough and the subsequent bleeding seeps through the tube and into the uterus.

TREATMENT

The practitioner must decide what the proper treatment of each case of bleeding is. He must first try to decide why the bleeding occurs and whether or not the problem is a medical one, as contrasted to surgery and radiation. If the bleeding is due to a blood disease, a lack of a normal component of blood coagulation, a vitamin deficiency or a hormonal disturbance, treatment can be undertaken along proper lines, but if such a diagnosis cannot be made, the patient should be treated as though the bleeding were due to malignant disease and a biopsy and curettage should be done. For medical treatment there are available estrin, progestin, testosterone, vitamin C, vitamin K, vitamin B and transfusion.

If the cause of the bleeding is not obvious, the patient must *not* be sent directly to the roentgenologist for x-ray treatment. This is a most important point. No roentgenologist, except under very exceptional circumstances, should attempt treatment with x-rays unless a diagnostic curettage and biopsy has been done. This is because x-ray treatment may stop the bleeding from a cancer and mask a serious situation. Roentgen therapy rarely cures cancer. Cases can be found where x-ray treatment has cured uterine cancer, but they are very few. The treatment of cervical cancer with x-ray alone, unless deliberately done and supplemented by vaginal-cone treatment, is wrong. X-ray treatment can prevent bleeding until the tumor has advanced to a much less treatable stage. If the cause of bleeding is in doubt, — and it usually is, — a biopsy of the cervix and endometrium should be done. Then, and then only, can x-ray treatment be correctly given for so-called "benign bleeding."

It is my opinion that ovarian function is worth preserving. Castration is followed by the menopause and its accompanying changes, such as vaginal atrophy, lack of interest in sex and alterations in the skin and bones. X-ray and radium treatment should be avoided when it is possible to remove the uterus and cervix and leave the ovaries in place. At the Pondville Hospital an ovary recently was seen with a fresh corpus luteum in it seventeen years after hysterectomy. It is easy for a surgeon to be biased, but having seen and cared for a great many patients that have had x-ray and radium therapy for benign bleeding, I am convinced that it is better, whenever possible, to save ovarian function.

A patient past the menopause should never be treated by radium and x-ray to stop bleeding. If a curettage does not reveal the cause of the bleeding, nothing more should be done. If the bleeding recurs it is best to curette again, and if it again recurs it is best to remove the uterus. X-ray treatment in moderate doses may prevent bleeding from cancer, and the treatment of cancer should be carried out as early as possible. Mistakes of this type have been observed in various clinics, and some patients are in a hopeless condition when seen, although they have had freedom from symptoms for definite periods of time. Cancer is curable in its early stages, but early recognition and adequate treatment are essential.

X-ray and radium should be reserved for the treatment of bleeding in spinsters near the menopause or for patients in such poor physical condition that they cannot stand a major surgical procedure. Surgery in a strong, healthy woman is safe, and the removal of the cervix is a boon to woman-

kind. Total hysterectomy with conservation of the ovaries is one of the most satisfactory of all surgical procedures.

SUMMARY

There are many reasons for uterine bleeding of the abnormal type. Care must be taken to rule in or out all the possibilities.

Some of the causes of bleeding are deficiency of normal blood-clotting components, hormonal dysfunction, vitamin deficiencies, injury to the sympathetic nervous system and blood diseases.

Benign and malignant tumors constitute the largest group of patients with abnormal bleeding.

No patient should be subjected to x-ray or radium treatment without proper histologic study of tissue from the cervix and endometrium.

Removal of the uterus and cervix, with conservation of the ovaries, is the proper treatment for patients with fibroids and benign tumors.

Cancers should be given their proper treatment, whether it is surgery, radium, x-ray or all these, undertreatment being worse than none.

Patients bleeding past the menopause should never be given x-ray or radium treatment until the bleeding has been adequately explained.

264 Beacon Street

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ADVANCES IN INHALATION THERAPY, WITH PARTICULAR REFERENCE TO CARDIORESPIRATORY DISEASE*

MAURICE S. SEGAL, M.D.†

BOSTON

THE present report centers particularly about the use of oxygen, helium-oxygen mixtures, inhalation sprays of bronchodilator, vasoconstrictor, aminophyllin and sulfonamide solutions and positive pressure therapy in a series of 49 cases of pulmonary or cardiac disease demonstrating anoxia, obstructive breathing or pulmonary edema, alone or in combination.

The effectiveness of inhalation therapy depends to a large extent on the type of equipment used. In the present study, the new B. E. M. (Barach-Eckman-Molomut¹⁻³) mask and the helium-oxygen hood apparatus^{4, 5} were used for the routine administration of oxygen or helium-oxygen mixtures. The mask can be used to deliver 40 to 95 per cent oxygen or helium-oxygen mixtures and is metered for positive pressure in the expiratory phase of respiration. The ventilated hood is the most effective apparatus for giving oxygen or helium-oxygen mixtures with increased pressures. Positive pressures up to 6 cm. of water can be applied to the inner surface of the lung during both inspiration and expiration. A detailed description and comparisons with other equipment have previously been published.⁶ For the administration of nebulized substances by the pulmonary route, the Vaponefrin nebulizer has proved most efficient. It produces a very fine, voluminous spray or smoke screen. The technic and value of employing continuous vaporization therapy may be found in papers by Barach and his associates,⁷⁻⁹ Lockey,¹⁰ Castex et al.,^{11, 12} Chambers et al.,¹³ Harris et al.,¹⁴ Norris,¹⁵ Stacey,¹⁶ Krueger et al.¹⁷ and the author.^{6, 18, 19, 29}

CLINICAL STUDY

Material

In this study 21 patients were treated for bronchial asthma, 6 for atypical pneumonia, 4 for bronchopneumonia in combination with organic heart disease and failure, 4 for pulmonary edema and anoxia associated with renal decompensation, 4 for pulmonary edema associated with acute left-ventricular failure, 3 for inhalational gas poisoning, 3 for chronic bronchiectasis, severe pulmonary emphysema and fibrosis, 1 for massive atelectasis of the entire right lung, 1 for atelectasis of the right lower lobe in association with severe rheumatic heart disease, cardiac failure and pregnancy, 1 for

respiratory obstruction following postoperative thyroidectomy, and 1 for rapid respiratory decompensation following splenectomy.

Fatal Cases

There were 12 deaths in this series. Autopsies proved that 8 cases were hopeless from the outset. This leaves a corrected mortality of 4 out of 41 cases, and it is questionable whether these could have been saved by any type of therapy. Two of these patients were moribund from the outset and survived only two days. Striking clinical improvement with relief of anoxia and obstructive manifestations were repeatedly observed, even though temporarily, in most of the fatal cases. A few typical case histories follow.

CASE 1. A 28-year-old woman with a diffuse, bilateral, virulent type of atypical pneumonia associated with lesions of the mucosa of the mouth and upper airways was moribund for a day before therapy was started. She regained consciousness and survived for 7 days in almost continuous residence in the hood apparatus. She died suddenly while being transferred from the hood to a tent apparatus.

CASE 2. A 48-year-old man with a diffuse bronchopneumonia following a subtotal gastrectomy demonstrated marked anoxia and pulmonary edema before he was placed in the hood apparatus. Conventional mask and tent oxygen therapy had been previously attempted without success. Within a period of 4 days, he responded successfully to a complete program of physiologically directed therapy and was comfortable and well without any further therapy. At that point, the abdominal stay sutures were removed and evisceration followed. The course thereafter was rapidly downhill and the patient died 3 days later. The autopsy revealed no ill effects from the sustained positive-pressure therapy.

CASE 3. A 43-year-old woman had a history of severe rheumatic heart disease of many years' standing. The terminal picture was characterized by repeated attacks of pulmonary edema, associated with a diffuse pneumonia. She was moribund at the outset and catheter, mask and tent oxygen had been of no avail. In the hood apparatus, she was given 100 per cent oxygen concentrations under positive pressures up to 5 cm. of water. The pulmonary edema was easily controlled in this way. She regained consciousness and for 2 days the prognosis was brighter. Death came suddenly on the 5th day of inhalation therapy. The autopsy revealed an almost completely stenosed mitral valve with a large vegetation filling the left auricle. The lungs showed little evidence of pulmonary edema, and there was no evidence of ill effects from the sustained positive pressures.

The pulmonary findings in the last case were the same as those found in the other two reported cases receiving positive pressures over periods of at least 4 days in the hood apparatus.

Living Cases

In the patients who survived, it was the opinion of many observers that death from respiratory decompensation was imminent in many of the cases. In the patients with atypical pneumonia, the hack-

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

From the First and Third Medical Services, Boston City Hospital, and the Department of Medicine, Tufts College Medical School.

†Assistant professor of medicine, Tufts College Medical School; junior visiting physician, Boston City Hospital; junior visiting physician, Beth Israel Hospital.

It is my opinion that ovarian function is worth preserving. Castration is followed by the menopause and its accompanying changes, such as vaginal atrophy, lack of interest in sex and alterations in the skin and bones. X-ray and radium treatment should be avoided when it is possible to remove the uterus and cervix and leave the ovaries in place. At the Pondville Hospital an ovary recently was seen with a fresh corpus luteum in it seventeen years after hysterectomy. It is easy for a surgeon to be biased, but having seen and cared for a great many patients that have had x-ray and radium therapy for benign bleeding, I am convinced that it is better, whenever possible, to save ovarian function.

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he degree of bronchospasm. I found that 1 per cent Neo-Synephrin was an effective vasoconstrictor of the tracheobronchial tree; it was particularly effective in controlling excessive secretions, as observed in cases of inhalational gas poisoning and some cases of atypical pneumonia and bronchial asthma. It can be effectively directed into the tracheotomy opening when necessary. It is a poor bronchodilator. Refractoriness to it usually does not develop. A slowing of the pulse rate may be observed. Occasionally, restoration of adrenalin sensitivity follows its use. Epinephrine is an effective bronchodilator. The Vaponefrin preparation was generally found to be the most effective. The combination of Neo-Synephrin and Vaponefrin was particularly effective in severe bronchospasm associated with profuse expectoration.

Continuous vaporization sprays of aminophyllin solutions were tried in a number of patients with bronchial asthma. Effective therapy may frequently be obtained with 0.5 to 0.7 gm. The volume of solution necessary and the expense involved militate against its general usage in this way, particularly when it is so effective rectally.

In a few patients with chronic bronchiectasis and pulmonary fibrosis, continuous vaporization sprays of 2.5 per cent sulfadiazine solutions were employed, generally preceded by Vaponefrin sprays. Negligible blood levels were generally obtained. Defervescence, diminution in the amount of sputum and general clinical improvement followed. In a striking case, a woman in the seventies with bilateral chronic bronchiectasis and pulmonary emphysema was able to leave the hospital after a week's treatment. Previously, she had been confined for many months.

It is difficult to evaluate the specificity of such therapy in a limited series, but the observations by other investigators have also been extremely encouraging. It appears that in patients with chronic bronchiectasis, an ideal technic is the combination of the following: nebulization of a microcrystalline suspension of sulfathiazole,¹⁴ use of oral iodides to decrease the viscosity of the secretions, addition of iodine¹⁵ to the sulfathiazole solution as an oxidizing agent¹⁶ to help destroy the inhibitory effects of para-aminobenzoic acid present in purulent exudates, and periodic bronchoscopic drainage.

Tracheotomies²⁹ were performed on many of the victims of the Coconut Grove disaster. These victims generally presented the picture of progressive anoxemia and obstructive respiratory disease. Tracheal edema as well as pulmonary edema was evident. It was generally believed by various observers that this procedure was performed too often, and in many cases with disastrous results. No one can deny its indication in selected cases with tracheal obstruction above the suprasternal notch, but in victims of gas inhalation the fundamental involvement is largely pulmonary.

Tracheotomized patients generally demonstrate persistent pulmonary fluid loss through the tracheotomy tube. This requires aspiration and suction at frequent intervals. Physiologically this procedure is unsound. These patients have lost the back pressure against the pulmonary capillaries that they are accustomed to. If tracheotomy must be performed, one should keep the opening dry and clear and apply positive-pressure inhalation therapy with proper humidification through the tracheal cannula.

In general, then, it is best to attempt a program of positive pressure, preferably with the ventilated or pressure hood apparatus, using mixtures of helium and oxygen, before resorting to tracheotomy in cases of tracheal obstruction, whatever the cause. The number of tracheotomies is minimized in this way.

SUMMARY

Physiologic directed inhalation therapy in the management of a consecutive series of 49 cases of pulmonary or cardiac disease demonstrating anoxia, obstructive breathing or pulmonary edema alone or in combination has been described.

There were 12 deaths. Eight of these cases were proved to have been hopeless from the outset, and it is questionable whether the other 4 patients could have been saved by any method of therapy. Many of the recovered patients were moribund at the outset, and the clinical improvement and recovery were striking.

The management of such cases included the following: oxygen or helium and oxygen mixtures, with or without positive pressures as indicated, using the B. E. M. mask and hood apparatus; repeated bronchial relaxation by the use of rectal aminophyllin, Dilaudid, iodides and vaporization with Neo-Synephrin and Vaponefrin; both the foregoing were carried out simultaneously or in part alone, depending on the circumstances.

Certain physiologic objections to tracheotomy have been presented.

Inhalation therapy is a most important adjunct in the therapy of serious cardiorespiratory disease, and the principles and equipment necessary should be more widely disseminated.

370 Commonwealth Avenue

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ing cough became less severe and more productive; in the patients with bronchial asthma, the total pulmonary ventilation was reduced and the vital capacities promptly increased; in the patients with pulmonary edema, the diffuse moist rales disappeared or diminished as long as the positive pressure was applied or until the original cause was removed; and in the patients with tracheal or tracheobronchial obstruction, there was a marked reduction in respiratory effort, particularly in inspiration, and respiratory failure was averted. Two case histories follow:

CASE 4. A middle-aged man was suffering from severe tracheal obstruction following the removal of a massive colloid goiter. Anoxia, cyanosis and marked inspiratory effort were apparent and a tracheotomy was to be performed. Shortly after a trial period of helium-oxygen breathing with positive pressure, the respiratory distress diminished, and within a few hours all signs of anoxia and suprasternal obstruction disappeared. The patient made an uneventful recovery.

CASE 5. A 52-year-old man with a complete atelectasis of the entire right lung that came on during convalescence from a severe atypical pneumonia was successfully managed with a complete program of physiologically directed therapy. When first seen, he was in severe pain and in mild shock. Anoxia, cyanosis and rapid respiratory failure seemed imminent. Pure oxygen under positive pressure brought relief. After a short trial, a mixture of 75 per cent helium and 25 per cent oxygen was substituted without the patient's knowledge. The relief was even more striking. Thereafter, for a period of 2 weeks he was treated intermittently with helium-oxygen mixtures and oxygen. He was discharged home after 1 month. The lung was completely expanded after 6 weeks, and he was able to resume his normal activities.

Treatment

The type of gas mixture used in these cases depended on the factors responsible for the dyspnea, whether anoxemia or respiratory obstruction. If anoxia was the main factor, oxygen in concentrations of 95 per cent or more was used alone with either the B. E. M. mask or hood. If respiratory obstruction or bronchial spasm predominated, mixtures of 70 to 75 per cent helium and 30 to 25 per cent oxygen were found more beneficial. These mixtures are about one third as heavy as air. Barach²⁰⁻²³ and Behnke²⁴ have demonstrated that an 80 per cent helium and 20 per cent oxygen mixture is from 30 to 50 per cent easier to breathe through constricted orifices than is air. Dean and Visscher²⁵ later demonstrated that in going from air to helium and oxygen in the laboratory animal with tracheal obstruction, there was 40 per cent reduction in the work of ventilation. In obstruction extended in a linear direction, however, the above physiologic advantages are reduced by the slightly increased viscosity of helium above that of nitrogen. Hence, helium should *not* be considered a panacea for all types of difficult breathing.

The more localized the obstruction the greater was the immediate relief observed. The relief in patients with status asthmaticus or in those with bronchospasm associated with atypical pneumonia or inhalational gas poisoning was generally prompt

and lasting. The majority of the patients with bronchial asthma were adrenalin fast and had not responded to repeated intravenous injections of aminophyllin, oxygen and sedation with morphine and paraldehyde. The earlier cases in this series were treated continuously with helium-oxygen mixtures. The later cases were treated intermittently with comparable results. In a few recent cases, I have followed Barach's²⁶ suggestion employing mixtures of nitrous oxide, helium and oxygen and have observed very effective relaxation.

Positive-pressure therapy, with either oxygen or helium-oxygen mixtures, was effectively administered through the B. E. M. mask, which is metered for positive pressure up to 4 cm. of water in the expiratory phase only, or in the hood apparatus during both inspiration and expiration. The application of a gentle internal distending force served to keep the bronchioles patent and opposed the hydrostatic pressure within the capillaries.²¹

In the cases of pulmonary edema, positive-pressure oxygen was employed in the expiratory phase of respiration with the mask apparatus and found most effective. In the cases with severe bronchospasm, a positive-pressure helium and oxygen mixture was employed in both phases of respiration with the hood apparatus. The best effect on bronchospasm was observed in the inspiratory phase of respiration.

Generally, positive pressures of 2 to 6 cm. of water were sufficient for preventing or treating pulmonary edema, but higher pressures were sometimes necessary for short periods. Pressures above 6 cm. of water in some cases diminish the return flow of blood to the right side of the heart. Theoretically, shock may be considered a contraindication to positive pressure. No difficulty is usually encountered if the lower pressures are used, beginning with 2 cm. of water and cautiously increasing the positive pressure as needed.

Some patients found such therapy tiring when the mask was used, and an occasional semiconscious patient at first became alarmed with the seemingly increased expiratory-phase resistance. Reassurance and rest generally overcame this. Wangenstein drainage or Miller-Abbott intubation was employed successfully in a few cases. This was carried out in both the mask and hood apparatus. Free, productive coughing and belching may be inhibited somewhat if therapy is continuous, hence rest periods are necessary.

Repeated bronchial relaxation was accomplished by the use of rectal aminophyllin, Dilaudid,* iodides, nebulization with Neo-Synephrin and Vaponefrin and proper humidification. A similar program has been described by Barach^{8, 9, 27, 28} and others.^{6, 18, 19, 29} Such a program is particularly effective in combination with helium-oxygen positive-pressure therapy, and its effectiveness varies directly with

*Barach²⁸ has used Demerol in approximately 20 cases of bronchial asthma, with results better than those with Dilaudid.

Price⁴ recorded a study of 224 children who had had single or multiple convulsions and were cared for by him as a member of a medical group that performed most of the medical service in a small city. With the history of parents and family and the obstetric, neonatal and pediatric histories at his command, he was able to assign etiologic factors to the convulsions that seemed adequate in all but about 12 per cent of the patients. This compared with an incidence of idiopathic convulsions about twice as great in Peterman's series of children coming to him solely because of convulsions. It must be remembered, however, that experience shows that the younger the patient the more probable is an etiologic explanation. Since the details of ages or the two series are not given by either author, it may be that comparison between them is unfair.

Postconvulsive pathology was investigated by Zimmerman⁵ in the brains of 16 children dying soon after severe convulsions. In all, loss of nerve cells on a noninflammatory basis had occurred. The cortex was involved in all cases, and in many the central gray matter and cerebellar nuclei in addition. Many of the patients had infectious diseases at the time of the convulsions, but especially striking was the case of a six-month-old patient who died of anoxia and convulsions thirty hours after accidental incision of the diaphragm during nephrectomy for tumor. Autopsy revealed an extensive pneumothorax and a widespread loss of cells from the cortex histologically similar to that found in the other cases. Zimmerman considered the cell injury to have been caused by anoxia and to have been the result, rather than the cause, of the convulsions. In the light of his findings, it is incumbent on the physician to take measures to combat anoxia during convulsions.

Penfield and Erickson⁶ published an encyclopedic study of epilepsy the main thesis of which was that convulsions can be divided according to their manifestations into fifteen types, many of which can be related to various parts of the brain (Table 1). Such a classification was useful to them in attempting to localize lesions amenable to surgical attack. It also directed attention to the well-known but often forgotten fact that convulsive cerebral discharges are not necessarily accompanied by motor phenomena and that pain or special sensory or visceral sensations are often the expression of such a discharge.

Wechsler⁷ published a study of a series of cases in which abdominal pain was the presenting symptom of intracranial neoplasms or abscesses that could be localized. The lesions involved the frontal, temporal or occipital cortex or the cerebellum or brain stem. Wechsler called attention to the fact that the most frequent aura of epilepsy is abdominal pain or discomfort and that in many cases abortive attacks consist only of such an aura. He also sug-

gested that the pain of hysteria may be real pain on a psychosomatic basis, the result of actual changes in brain physiology.

Bridge, Livingston and Tietze⁸ reported a study of 83 children who were brought to the hospital suffering from breath-holding spells. The incidence of such spells in a clinic population was also investigated. It was found that there was no sharp division between simple tempers and breath holding, but

TABLE 1. *Types of Convulsions in Epilepsy (Penfield and Erickson⁶).*

CLINICAL TYPE	LOCALIZATION
Somatic motor manifestations:	
Generalized seizure (grand mal)	Complete motor area
Jacksonian (local motor) seizure	Prerolandic gyrus
Masticatory seizure	Lower rolandic area
Simple adverse seizure	Frontal area
Tonic postural seizure	
(decerebrate, opisthotonos)	
brain stem	
Somatic sensory manifestations:	
Somatosensory seizure	Postrolandic gyrus
Visual seizure	Occipital area
Auditory seizure	Temporal area
Vertiginous seizure	Temporal area
Olfactory seizure	Infratemporal area
Visceral manifestations:	
Autonomic seizure	Diencephalic area
Psychical manifestations:	
Dreamy state	Temporal area
Petit mal	
Automatism (ictal and postictal)	
Psychotic states (secondary)	

it was also true that in the children admitted with a complaint of breath holding the manifestations were much severer than in the clinic patients not complaining of them. A preceding circumstance arousing a violent emotional response was an essential part of a breath-holding spell, especially frequent causes being pain and anger. Following the stimulus the child sometimes took a breath or two, crying loudly, and then became rigid all over, holding his breath in expiration. In five or ten seconds cyanosis resulted, about twenty seconds caused severe cyanosis and unconsciousness with a fall to the floor, and thirty or forty seconds of breath holding usually resulted in convulsive phenomena, either generalized or localized. Following the attacks the children were confused or drowsy and more or less exhausted in proportion to the severity of the attack.

Follow-up studies were made on 51 patients at an average age of eleven years. The average age at onset had been about one year and the average age at recovery had been about four years, but there was a wide range. Practically all the children had outgrown the breath-holding habit by the time they were ready for the first grade. Mentally retarded children clung to the habit longer than did normal children. Of the 83 original patients, 3 had had recurrent convulsions prior to the breath-holding attacks, 2 had epilepsy when seen for follow-up, and 2 were thought to have it although the diagnosis was not absolutely proved. This represents an incidence of 8 per cent, a considerable increase over Thom's finding in his large group of unselected chil-

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MEDICAL PROGRESS

EPILEPSY AND CONVULSIONS IN CHILDHOOD

RANDOLPH K. BYERS, M.D.*

BOSTON

SINCE no satisfactory method of differentiating so-called "simple convulsions" of childhood from epilepsy exists, it is necessary to consider together the entire group of convulsive disorders. A study by Thom¹ demonstrated clearly the close relation that exists between the two heretofore artificially separated groups. He made a comparison of the incidence of epilepsy over a period of years in 8000 unselected children first seen in a well-baby clinic and 395 children seen because of infantile convulsions. Of the former less than 1 per cent developed epilepsy during the follow-up period, whereas of the latter 12 per cent were definitely epileptic at the end of the study. In particular, Thom found that convulsions recurring over a period of weeks or months were likelier to be followed by epilepsy than was a single convulsion or a series of convulsions occurring within a relatively short period of hours or days. In his experience so-called "idiopathic convulsions" were likelier to merge into a chronic convulsive disorder than were those of any other group except those cases in which there was manifest brain damage. Petit-mal attacks occurring in the first two years of life were likely to merge into epilepsy or to become associated with mental retardation. Convulsions of themselves might cause cerebral damage affecting brain development and subsequent mental development. A bibliography of similar and related studies is appended to his article.

*Instructor in pediatrics, Harvard Medical School; associate visiting physician, Children's Hospital.

A study by Peterman,² also of a large group of children subject to convulsions, added evidence tending in the same direction. He pointed out that on electroencephalography a large percentage of such children showed what he interpreted as a cerebral dysrhythmia. Since standards for normal children of the younger age group have not yet been thoroughly evolved, it may be necessary to modify Peterman's figures, but there can be little doubt about the general conclusion, namely, that the cerebral physiology of children subject to convulsions is different in many cases from that of normal children.

On the other hand, evidence that the infantile nervous system responds to imposed stresses by convulsions more easily than the adult nervous system was obtained by Wegman.³ He elevated the body temperature of cats and kittens in a radiant-heat chamber and found that a rapid rise in body temperature was followed by convulsions much more frequently in kittens than in cats. A slow rise in temperature was seldom followed by convulsions. Neuropathologic changes were found that varied somewhat in relation to the rate of temperature rise. These findings suggested that convulsions may be produced in childhood by stresses that would be ineffective in adulthood. On the other hand, it may well be that neuropathologic changes can be produced either by the causative agent or by the convulsion itself, tending to lower the convulsive threshold in later life.

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Correction. In the progress report "Recent Advances in Surgery" by Dr. Alfred Blalock, which appeared in the August 17 issue of the *Journal*, the word "any" in the sixth line from the bottom of the second column on page 266 should be changed to "many."

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30421

PRESENTATION OF CASE

A thirty-one-year-old housewife entered the hospital because of pain in the abdomen and constipation.

The patient had been in apparent good health until ten days before entry, when she developed crampy, intermittent pain in the left lower quadrant of the abdomen. She passed no gas or feces by rectum despite repeated cathartics and enemas. She became increasingly anorexic, but had no nausea or vomiting. On the day before admission, after taking a liquid cathartic, she experienced severe pain in the abdomen, which required morphine. She had had an appendectomy five years before admission. She had always been somewhat constipated, but never had any rectal bleeding. The menstrual periods had been regular, the last period occurring three weeks before entry. There had been no weight loss.

Physical examination showed a well-developed, slightly obese woman, complaining of pain in the left lower quadrant. The heart and lungs were normal. A low, well-healed, midline abdominal scar was present. Two dilated loops of intestine could be seen running obliquely across the abdomen.

*On leave of absence

There was tenderness, with slight spasm, in the left lower quadrant, but no rebound or cough tenderness. Bursts of high-pitched peristalsis were heard accompanying the bouts of pain.

The blood pressure was 110 systolic, 60 diastolic. The temperature was 100°F., the pulse 86, and the respirations 22.

Examination of the blood showed a white-cell count of 12,000. The urine was alkaline, with a specific gravity of 1.012; 2 or 3 white cells per high-power field were seen in the sediment. A blood Hinton test was negative. A plain film of the abdomen showed a single loop of dilated large intestine, apparently extending up from the sigmoid. A small amount of gas was scattered through the remainder of the large intestine. A barium enema (Fig. 1) showed the barium to fill as far as the rectosigmoid junction, at which point there was a definite twist of the mucosa. A small amount of barium passed into the sigmoid, which was markedly dilated.

Shortly after admission an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS D. MOORE: This case at first glance, and indeed at second glance, looks fairly simple. For that reason it probably has some hidden hurdle. A thirty-one-year-old patient who had had intestinal obstruction for ten days came into the hospital. The question of which bowel was involved is of prime importance. We have good evidence that it was large-bowel obstruction. In the first place, she had been obstructed for ten days but was not extremely sick. In the second place, pain and obstipation had gone on for days without any nausea or vomiting. Both those facts suggest large-bowel rather than small-bowel obstruction. She had a severe bout of pain when she took a cathartic,

dren followed for a longer period. In addition, behavior disturbances were extremely frequent in this group of children. It thus appears that children subject to severe breath-holding spells tend to be less satisfactory subjects than do unselected ones, but that by and large their chances of developing serious aftereffects are small.

From the point of view of treatment, several of the previously mentioned articles give valuable suggestions. Peterman² pointed out that the convulsion per se tended to raise the body temperature, with possible damage to the brain, and that hence the time-honored hot bath, even though not hot enough to burn the skin, tended to increase the already rising temperature. He recommended cool sponging, sodium phenobarbital subcutaneously, chloroform or vinyl ether by inhalation, if needed in addition, and clearing the airway in acute emergencies. He considered a ketogenic diet the most effective treatment. He added that accurate diagnosis is essential for correct treatment.

Penfield and Erickson⁶ covered the treatment of convulsions and epilepsy thoroughly from both the medical and the surgical point of view; their book should be consulted for details. An important point mentioned by them was that morphine has extremely poor anticonvulsant properties and that since it is a respiratory depressant it may make the anoxia worse and is contraindicated in convulsions.

Price, Waelsch and Putnam⁹ described the usefulness of racemic glutamic acid hydrochloride in epilepsy associated with slow waves in the electroencephalogram, that is, in petit-mal and psychomotor attacks. It was ineffective in grand mal. The dosage was controlled by the reaction of the urine, an attempt being made to maintain it at a level of pH 4.5 to 5.0, as measured with nitrazine papers. Increased physical and mental alertness was a most gratifying result noted by parents, teachers and physicians.

Supplies of this drug are not as yet on the market, but it is being distributed through a few teaching hospitals. A small number of cases of petit mal treated at the Children's Hospital have shown marked reduction or suppression, and in most cases improvement in the patient's mental attitude and personality has been striking. The patients so treated are still small in numbers, and chance may well have been important in influencing the results.

Sodium diphenylhydantoin was introduced for the control of convulsions by Merritt and Putnam^{10, 11} after a series of experiments in the control of artificially induced convulsions in cats by a number of related compounds. They found it effective in a group of epileptic patients in whom other drugs had been useless. Petersen and Keith¹² found that of 59 patients previously treated unsuccessfully with phenobarbital or bromide, 8 per cent were completely relieved of their attacks, and another 61 per

cent were greatly improved both as to frequency of attacks and as to sense of well-being.

Lennox¹³ reviewed the drug treatment of epilepsy and concluded that diphenylhydantoin sodium (Dilantin sodium) is the drug of choice, both because it is more effective than other drugs in controlling attacks and because it is much freer from hypnotic effects than are the sedative drugs. In his experience it was most effective in psychic attacks, less so in grand mal and least effective in petit mal. He listed its toxic effects as gastric, dermatologic, gingival and neurologic. The unpleasant gastric symptoms were benefited by giving the drug after meals. The dermatitis was usually mild and tended to regress in the milder cases if the drug was temporarily discontinued and resumed in smaller doses, with a gradual increase to an effective level. Gingival hyperplasia was occasionally seen and caused little discomfort. It seemed not to be related to scurvy, as had been suggested. Neurologic disturbances, such as tremor and ataxia, could usually be controlled by reduction of the dosage, but in a few cases psychologic symptoms, such as hallucinations and maniacal states, tended to recur no matter how cautiously the drug was exhibited.

Regarding the actual use of the drug, Lennox pointed out that it is of the utmost importance, as with all other forms of treatment, to have an accurate record of the incidence of seizures before commencing it. In changing to this drug from one of the sedative drugs, he considered it important to reduce the dosage of the latter slowly over a period of weeks. He recommended beginning the use of diphenylhydantoin sodium at a level of 0.03 gm. ($\frac{1}{2}$ gr.) twice a day for children under four years, the initial dose for older children being progressively more up to 0.1 gm. ($1\frac{1}{2}$ gr.) three times a day for those of approximately adult size. The dosage was to be increased until the attacks were controlled or toxic symptoms appeared. In children of six the upper limit of dosage was about 0.4 gm. (6 gr.) daily, and at adult levels the upper limit was 0.6 gm. (9 gr.) daily. The drug was dispensed in 0.1-gm. ($1\frac{1}{2}$ gr.) and 0.03-gm. ($\frac{1}{2}$ -gr.) capsules. For those unable to swallow the capsules Lennox recommended mixing the powder from the capsules with a little cream to cover its bitter taste.

Lennox made a plea for honesty in the prescription of all drugs and their discontinuance unless they accomplished a definite reduction in seizures or an important psychologic improvement.

319 Longwood Avenue

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that there was visible peristaltic activity indicated in the sentence, "Two dilated loops of intestine could be seen running obliquely across the abdomen," simply indicates that the bowel was dilated enough to be seen through the abdominal wall.

The laboratory work is not too helpful. Evidently the patient was not particularly dehydrated, since the specific gravity of the urine was only 1.012 — another point suggesting large-bowel rather than all-bowel obstruction. It would be interesting to know what a guaiac or benzidine test on the stool contents showed.

To summarize, we have a thirty-one-year-old woman, who, without previous symptoms, developed the symptoms and signs of large-bowel obstruction. The most frequent cause of such a situation is carcinoma, and this ought to be regarded as carcinoma until good evidence shows it to have been due to something else. One might say that this patient was too young for a carcinoma. She was young, but about a year or so ago Dr. Cope discussed a case here in which a boy of fourteen had a colloid carcinoma in the region of the splenic flexure. Therefore, her age does not rule it out. The sclerosing annular type of carcinoma of the sigmoid can often cause obstruction as its first symptom, since bleeding may only be occult, and anal or rectal symptoms may be absent.

What other conditions could have given this history? A diverticulitis can obstruct the large bowel, but one would expect some story of large-bowel difficulty over a period of years. Also, it is unusual for obstruction to be a predominant feature in diverticulitis, an inflammatory sort of reaction generally being more prominent. An endometriosis of the large bowel may obstruct, but one would not expect to be told that the menstrual periods were ineffectual.

Can an extrinsic band obstruct the large bowel as it so often obstructs the small bowel? The answer is, No; simply because large-bowel peristalsis is usually powerful enough to overcome a benign cicatricial stenosis or extrinsic band. Occasionally, stenosis subsequent to lymphopathia venereum or radiation is obstructing, but we have no evidence for either in this case.

How about volvulus? That is a condition that can obstruct the large bowel. It certainly is unusual in a woman of thirty-one, and I have already said that I think this ought to be considered cancer until proved otherwise. But I think the x-ray studies have "proved it otherwise"; in fact, I believe that the x-ray films are pathognomonic of volvulus. The barium running up and coming to a sharp point strengthens the argument for volvulus, and as Dr. Schulz said, the barium picture itself suggests a twist. The other point, as I have already mentioned, is that the degree of dilatation is so great that one suspects a loop obstructed at both ends,

and volvulus and internal hernia are about the only situations that produce obstruction of bowel at both ends of the loop. So I believe that we have good evidence that this patient had a volvulus of the sigmoid, supposedly due to the chance twisting of a congenitally long sigmoid mesocolon.

CLINICAL DIAGNOSIS

Volvulus of sigmoid.

DR. MOORE'S DIAGNOSIS

Volvulus of sigmoid.

ANATOMICAL DIAGNOSIS

Volvulus of sigmoid.

PATHOLOGICAL DISCUSSION

DR. RONALD C. SNIFFEN: Dr. Scannell, will you say a word or two about the operation?

DR. JOHN G. SCANNELL: I helped Dr. Munro operate, and the findings that Dr. Moore foretold were found. At operation the bowel, as I remember it, was twisted two and a half times. It was large and edematous. It was reduced, and a complementary cecostomy was performed. Twelve days later, the sigmoid was resected.

DR. SNIFFEN: Dr. Munro removed about 24 cm. of sigmoid colon. Externally it looked quite normal, apart from slight dilatation. Internally it was intriguing in that a fold of mucosa and bowel wall protruded into the lumen, looking much like a venous valve. Kinking of the sigmoid had apparently occurred some time in the past, and following this, fusion of the adjacent peritoneal surfaces by fibrous adhesions, thus producing a permanent infolding of the wall.

DR. MOORE: What was the relation of this "valve" to the volvulus? Did it seem to have anything to do with initiating the twist?

DR. SNIFFEN: The "valve" was approximately in the middle of the segment of sigmoid. Of course, when we received the specimen, there was no volvulus and the dilatation had subsided.

Microscopically the bowel wall was normal.

CASE 30422

PRESENTATION OF CASE

A seventy-one-year-old retired physician entered the hospital because of abdominal pain.

The patient had been in good health until four years before entry, when he had a combined abdominoperineal resection for carcinoma of the rectum in a community hospital. He was well until about one year before admission, at which time, following several attacks simulating gall-bladder disease, a cholecystectomy was performed, which gave complete relief. He remained asymptomatic until three days prior to entry when, after a heavy

which is also characteristic of large-bowel obstruction.

Let us see the x-ray films.

DR. MILFORD SCHULZ: The striking thing about the plain film is the large loop of gas-filled bowel that seems to rise out of the pelvis and to taper off to a point at its lower margin. After the intro-

structed at both ends, making a so-called "trapped loop." The dilatation, which I estimate to approach 15 cm. in diameter, is way out of the range of even a markedly dilated portion of small bowel. There is some gas in this film, which I should guess is in the cecum. Do you agree with that, Dr. Schulz?

DR. SCHULZ: Yes.



FIGURE 1. Roentgenogram Following the Barium Enema.
Note the dilated sigmoid (retouched).

duction of barium by rectum (Fig. 1), we see this tremendously dilated loop of bowel rising out of the pelvis, and a narrow area in the midsigmoid where it looks as though the bowel had been twisted on itself.

DR. MOORE: Dr. Schulz does not want to make it too easy for me. The x-ray films fit in with the concept that this was primarily large-bowel obstruction. In the first place, the large size of the loop is thoroughly compatible with an obstructed loop of large bowel, especially if the loop was ob-

DR. MOORE: That is further evidence that this was large-bowel obstruction, because in small-bowel obstruction after ten days one would not expect to find any gas in the large bowel.

Other features of the history are more or less non-contributory and I shall not go over them in detail. The physical examination was most significant in that the record states that the patient did not look particularly ill, a finding, as previously mentioned, that is not compatible with ten days of complete small-bowel obstruction. The

that there was visible peristaltic activity indicated in the sentence, "Two dilated loops of intestine could be seen running obliquely across the abdomen," simply indicates that the bowel was dilated enough to be seen through the abdominal wall.

The laboratory work is not too helpful. Evidently the patient was not particularly dehydrated, since specific gravity of the urine was only 1.012 — a point suggesting large-bowel rather than small-bowel obstruction. It would be interesting to know what a guaiac or benzidine test on the fecal contents showed.

To summarize, we have a thirty-one-year-old man, who, without previous symptoms, developed symptoms and signs of large-bowel obstruction. The most frequent cause of such a situation is carcinoma, and this ought to be regarded as carcinoma until good evidence shows it to have been due to something else. One might say that this patient is too young for a carcinoma. She was young, it is about a year or so ago Dr. Cope discussed a case here in which a boy of fourteen had a colloid carcinoma in the region of the splenic flexure. Therefore, her age does not rule it out. The sclerosing intussusception type of carcinoma of the sigmoid can often cause obstruction as its first symptom, since bleeding may only be occult, and anal or rectal symptoms may be absent.

What other conditions could have given this history? A diverticulitis can obstruct the large bowel, but one would expect some story of large-bowel difficulty over a period of years. Also, it is unusual for obstruction to be a predominant feature in diverticulitis, an inflammatory sort of reaction generally being more prominent. An endometriosis of the large bowel may obstruct, but one would not expect to be told that the menstrual periods were ineffectual.

Can an extrinsic band obstruct the large bowel as it so often obstructs the small bowel? The answer is, No; simply because large-bowel peristalsis is usually powerful enough to overcome a benign cicatricial stenosis or extrinsic band. Occasionally, stenosis subsequent to lymphopathia venereum or radiation is obstructing, but we have no evidence for either in this case.

How about volvulus? That is a condition that can obstruct the large bowel. It certainly is unusual in a woman of thirty-one, and I have already said that I think this ought to be considered cancer until proved otherwise. But I think the x-ray studies have "proved it otherwise"; in fact, I believe that the x-ray films are pathognomonic of volvulus. The barium running up and coming to a sharp point strengthens the argument for volvulus, and as Dr. Schulz said, the barium picture itself suggests a twist. The other point, as I have already mentioned, is that the degree of dilatation is so great that one suspects a loop obstructed at both ends,

and volvulus and internal hernia are about the only situations that produce obstruction of bowel at both ends of the loop. So I believe that we have good evidence that this patient had a volvulus of the sigmoid, supposedly due to the chance twisting of a congenitally long sigmoid mesocolon.

CLINICAL DIAGNOSIS

Volvulus of sigmoid.

DR. MOORE'S DIAGNOSIS

Volvulus of sigmoid.

ANATOMICAL DIAGNOSIS

Volvulus of sigmoid.

PATHOLOGICAL DISCUSSION

DR. RONALD C. SNIFFEN: Dr. Scannell, will you say a word or two about the operation?

DR. JOHN G. SCANNELL: I helped Dr. Munro operate, and the findings that Dr. Moore foretold were found. At operation the bowel, as I remember it, was twisted two and a half times. It was large and edematous. It was reduced, and a complementary cecostomy was performed. Twelve days later, the sigmoid was resected.

DR. SNIFFEN: Dr. Munro removed about 24 cm. of sigmoid colon. Externally it looked quite normal, apart from slight dilatation. Internally it was intriguing in that a fold of mucosa and bowel wall protruded into the lumen, looking much like a venous valve. Kinking of the sigmoid had apparently occurred some time in the past, and following this, fusion of the adjacent peritoneal surfaces by fibrous adhesions, thus producing a permanent infolding of the wall.

DR. MOORE: What was the relation of this "valve" to the volvulus? Did it seem to have anything to do with initiating the twist?

DR. SNIFFEN: The "valve" was approximately in the middle of the segment of sigmoid. Of course, when we received the specimen, there was no volvulus and the dilatation had subsided.

Microscopically the bowel wall was normal.

CASE 30422

PRESENTATION OF CASE

A seventy-one-year-old retired physician entered the hospital because of abdominal pain.

The patient had been in good health until four years before entry, when he had a combined abdominoperineal resection for carcinoma of the rectum in a community hospital. He was well until about one year before admission, at which time, following several attacks simulating gall-bladder disease, a cholecystectomy was performed, which gave complete relief. He remained asymptomatic until three days prior to entry when, after a heavy

dinner, he had "an upset stomach." An attempt to use warm water as a laxative made him vomit once or twice. Some time later he developed pain in the right lower quadrant requiring morphine. The bowel movements, which had previously been normal, ceased entirely. There had been no recent weight loss. He was unable to take anything by mouth until the day of admission, when he retained sips of water. No other information was available.

The past history was otherwise noncontributory.

Physical examination showed a well-developed, well-nourished man in slight distress. The heart and lungs were normal. The abdomen presented scars of the gall bladder and combined abdominoperineal operations and a colostomy. There was a large, tender mass filling the right abdomen. The mass was somewhat dull to percussion.

The blood pressure was 152 systolic, 86 diastolic. The temperature was 97°F., the pulse 90, and the respirations 15.

Examination of the blood showed a white-cell count of 10,500. The nonprotein nitrogen was 70 mg. per 100 cc., and the protein 5.8 gm. The chloride was 87 milliequiv. per liter. A plain film of the abdomen showed dilated loops of small intestine in the midportion and left side of the abdomen. The cecum was filled with fecal matter, and there was a considerable amount of gas in the transverse colon and splenic flexure. No gas was seen in the region of the pelvis.

A few hours after admission an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. GORDON A. DONALDSON: I might say at the outset that I shall accept the fact that this man had gall-bladder disease, perhaps stones and that he was completely relieved by cholecystectomy.

There are several points in the history, as you might guess, that I should like to have in order to make a diagnosis. I suspect that the patient was too ill to give any further points that might be helpful. The brevity of the physical examination, however, I am at a loss to explain. For instance, I should like to know about peristalsis. Too often the use of the stethoscope by the surgeon is overlooked. The absence or presence and type of peristalsis would be of tremendous help in this particular case. I should also like to know more about the nature of the mass in the right lower quadrant—whether it extended to the flank, whether it had an edge, and just how tender it was. It is merely stated that he had pain in the right lower quadrant. It would have been of help, I think, to have examined the patient through the colostomy to see if anything could be felt within the abdomen. I shall have to work, however, with what I have.

A few points are definite, and I must say that some of them disturb me. In the first place, the sequence of vomiting followed by pain is unusual.

I should guess that the vomiting was reflex in origin at the outset, starting in the region of the ileocecal valve. This went on into persistent vomiting as a result of small-bowel dilatation. Whatever the patient had, then, lay in the region of the ileocecal valve and later precipitated small-bowel obstruction.

The laboratory data are consistent with the history of three days' obstruction. I think the elevation in white-cell count was probably due to moderate degree of dehydration. The nonprotein nitrogen was slightly high, which can be explained on the same basis. The total protein was perhaps rather low, but the patient might well have had liver that was not functioning properly. The blood chloride level was consistent with the story of vomiting. As to the chart, the pulse was low for a degree of severe intestinal obstruction; the temperature was consistent with a noninflammatory process.

I think that we might gain a great deal by looking at the x-ray films.

DR. MILFORD SCHULZ: On this film you see several rather widely dilated loops of small bowel. There is no gas or feces in the distal half of the colon, but there is quite a bit of gas and fecal matter in the cecum.

DR. DONALDSON: There is more gas in the cecum than I had counted on; perhaps this can be accounted for by a self-administered enema.

Can you outline a mass?

DR. SCHULZ: I cannot see a definite mass in the abdomen.

DR. DONALDSON: Can you outline the liver edge?

DR. SCHULZ: No; it probably comes down to just above the splenic flexure, as indicated by the gas-filled bowel. One really cannot see the liver edge except in so far as the bowel is adjacent to it.

DR. DONALDSON: I should say that the small bowel is diffusely dilated to a rather severe degree.

DR. SCHULZ: Yes; curiously enough there is not a great deal of dilatation in the right lower quadrant, but the bowel may be filled with fluid and not evident.

DR. DONALDSON: The positive evidence in this case is disconcerting. In the first place, I doubt that the dilatation in the right lower quadrant was due to an inflammatory process. It is unlikely that the patient had had a vascular accident in the bowel, in view of the relatively low white-cell count and the type of pain. He could have had, of course, a retroperitoneal recurrence of malignant disease in the abdominal cavity; but that also is unlikely, although a possibility. It is strange that the physician noted a sizable mass in the right lower quadrant. From the x-ray film, I should guess that the liver as a source of this mass is ruled out.

We then come down to the fact that the likeliest cause for this mass is bowel. In any combined abdominal resection in which the upper sigmoid is not sutured to the lateral abdominal wall it is always possible for the bowel subsequently to herniate

through the opening in the left gutter and to go into the lower abdomen, possibly extending into the right abdomen. Such a condition is consistent with the x-ray findings. I must say that I am not too satisfied with that diagnosis because I could expect that there would have been more loops of small bowel in the right lower quadrant. Traction on the sigmoid the small bowel would cause obstruction distal to the splenic flexure, which would produce gas in the proximal large bowel.

DR. RONALD C. SNIFFEN: Dr. McKittrick, will you tell us about your findings.

DR. LELAND S. MCKITTRICK: First of all, I am clear what Dr. Donaldson's diagnosis is.

DR. DONALDSON: Bowel volvulus.

DR. MCKITTRICK: What do you mean by "bowel volvulus"?

DR. DONALDSON: I think that the bowel had herniated down through a trap in the left gutter, thus presenting itself in the right lower quadrant.

DR. OLIVER B. COPE: Do you mean the small intestine — a small-intestine volvulus? You made the statement that the bowel was distended to the splenic flexure.

DR. DONALDSON: I think that in rotating the small bowel produced obstruction in the colon.

DR. MCKITTRICK: I was greatly impressed and rather disconcerted by the confidence with which Dr. Donaldson anticipated seeing the x-ray films, because I rarely have any films shown to me at these conferences that do not add to my confusion. Something about them always seems to mix me up.

DR. DONALDSON: I was looking for help in the history.

DR. MCKITTRICK: And you did not get it.

DR. DONALDSON: No.

DR. SNIFFEN: Dr. McKittrick, can you answer any of Dr. Donaldson's questions?

DR. MCKITTRICK: I cannot. One of them was particularly pertinent. I am open to criticism because I did not listen with a stethoscope and consequently do not know whether the patient had peristaltic sounds. Dr. Moore probably did listen to the abdomen and can give an answer.

DR. FRANCIS D. MOORE: There was no evidence of peristalsis, but the patient had been obstructed for three and a half or four days.

DR. MCKITTRICK: There was a definite large mass filling the right lower quadrant, just as the transcript says. It was tender and surprisingly firm. Before these x-ray examinations I thought that the patient had an acute obstruction of the small bowel. Then when I looked at the x-ray films and saw the gas in the large bowel, it was a bit disturbing because it really did not fit in with what I thought the x-ray films should have shown. Since he had an acute illness of three days' duration, had passed no gas through the colostomy and had a tender mass in the right lower quadrant, it seemed to me that he had

a strangulated small bowel. I did not know quite how to explain the findings in any other way, and it was on that basis that he was operated on.

CLINICAL DIAGNOSIS (PREOPERATIVE)

Strangulated small bowel.

DR. DONALDSON'S DIAGNOSIS

Small-bowel volvulus.

ANATOMICAL DIAGNOSIS

Small-bowel volvulus.

PATHOLOGICAL DISCUSSION

DR. MCKITTRICK: At operation, when the abdomen was opened, which we did through a right incision, all one could see was strangulated bowel. The mass that we had felt was strangulated bowel, and I still do not understand how it could have been so firm. I believe that I have never felt intestine that was so firm and tense as this small bowel was. It was shiny and quite discolored. He did have a volvulus, and the lateral gutter was still obliterated. Dr. Donaldson was perfectly right: the patient simply had a twist of the small bowel at its mesentery, and there was a fixed point that had to be freed before it could be untwisted. We made an enormous incision — practically from one end of the abdomen to the other — in order to untwist the bowel without rupturing it. The color improved a bit as we watched it, and we put it back without any further manipulation because it seemed to me that there was no possibility of getting him by if we attempted major resection. We had to run the chance that this was viable bowel, even though we thought the prognosis was bad. At the end of operation the patient was in excellent condition.

DR. SNIFFEN: Do you believe that any of the adhesions from the previous operations initiated the volvulus?

DR. MCKITTRICK: I do not quite see how they could have. There was no definite point of obstruction because of a constricting band. Why the intestine had twisted is beyond me. There were a couple of fixed points, however, that probably had something to do with it. The interpretation of the mechanism of an acute small-bowel obstruction has always been a difficult thing for me, and I do not know just how to interpret this. We know that the gutter was still completely obliterated.

DR. DONALDSON: Is it not unusual to have that amount of gas in the large bowel?

DR. MCKITTRICK: Yes, but he may have taken an enema as you suggested. That would put air in the large bowel.

DR. SNIFFEN: This man died about ten hours after operation. The essential finding was early gangrene of the lower jejunum and upper ileum for a distance of approximately 250 cm. There was no acute

peritonitis, although about 300 cc. of blood-tinged fluid had spilled into the peritoneal cavity. The various loops were bound together by old fibrous adhesions. The mucosa was intact in the involved intestine, and the wall seemed viable, although it was deep red. Its mesentery was not long and measured only 12 cm., the average length of the mesentery of the small intestine being about 20 cm. The mesenteric arteries and veins were patent throughout. On microscopic section there was no definite histologic evidence of cell necrosis, although there was quite severe hemorrhage into the wall. There were extensive hemorrhage and edema in the lungs. We found no cancer, and the colostomy was in good repair.

DR. McKITTRICK: I do not quite know why this patient died. He was in surprisingly good shape at the end of operation, and although I thought

that he was going to die, I was surprised that he died so soon after operation.

DR. SNIFFEN: The pulmonary edema and hemorrhage were quite marked. We could find no obvious mechanical reason for the twist.

DR. McKITTRICK, in operating on volvulus, how often do you resect the loop at the first operation?

DR. McKITTRICK: If badly obstructed, one would not resect the loop unless the bowel was nonviable. In large-bowel volvulus an experienced surgeon, if the setup is just right, occasionally removes the involved bowel, but it adds to the risk of operation.

DR. SNIFFEN: Do you advocate removing it if there is an unduly long mesentery?

DR. McKITTRICK: We have done that not infrequently in large-bowel volvulus, but in most cases as an elective procedure after we have taken care of the mechanical obstruction.

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MASSACHUSETTS, THERE SHE STANDS

THIS country has lapsed into that dangerous period of its long struggle for victory in which it has become overly war-weary; like a fighting team that has trained zealously and enthusiastically for its great effort, it has gone stale. We need not compare ourselves with England, two years longer at war than we have been, or with Russia, a year ahead of us in the conflict, or with China; after eight years of the struggle, or with Germany. The case is different; they have either been faced with doom from the beginning if they relaxed or, after tasting victory, have seen the inevitability of defeat gradually shaping itself.

The temperamental citizenry of our somewhat emotional nation has been too far from the thunder of the big guns. It has seen victory around each corner since the close of the campaign in North Africa, its natural, if somewhat immature, ebullience being daily stimulated by the eruptions of the pollyannas of press and radio, who dare not tell the truth lest the people become discouraged.

Each paean of triumph has had its damaging effect on the war effort. Fresh thousands have left the essential industries to find shelter in more permanent, if less lucrative, occupations; municipal solons are planning their several V-Day celebrations with the utmost gravity and in the minutest detail; G. I. Joe himself, we are told by certain of the less feverish correspondents, is becoming disheartened by the fact that all is not over, despite the prognostications of the armchair board of strategy. There has been too much talk about who gets home first when the war is over, and we are only now coming far enough out of Dreamland to realize that the war will not be over until the fighting stops, which may not be for a long time to come. Hitler could not have planned a better propaganda campaign to soften his forthcoming, if delayed, defeat.

A sign of the slackening war interest here at home that strikes close to the healing fraternity is the easy professional virtue that lends itself to an increasing prescription of extra rations for a self-indulgent public of doubtful patriotic fervor. Perhaps our sons and brothers before the Siegfried line or on the Pacific island beaches will die happier in the knowledge that Cousin Annie has had a slice of sirloin for her lunch or that Uncle Jim can have an extra bit of butter for his bread. No doubt an awareness, by their occupants, of the fact that fuel oil is flowing more freely on the Atlantic seaboard will make a few thousand dugouts on the western bank of the Rhine seem positively cozy this winter. Something more than medical necessity is needed to explain the certificates for extra rations that are being sent for review in this state, in addition to those granted by local boards, at the rate of a thousand a month.

God save the Commonwealth of Massachusetts!

CHEMOTHERAPY OF WOUNDS AND BURNS

In May, 1943, the Subcommittee on Surgical Infections of the National Research Council and the responsible investigators of the Contaminated Wound and Burn Project operating under the supervision of the Committee of Medical Research of the Office of Scientific Research and Development¹ presented before the American Surgical Association the results of a study on the prevention of infection in contaminated accidental wounds, compound fractures and burns. This report covered some 1500 cases collected subsequent to February, 1942.

Several points made in the introduction of the report are worthy of comment. A period of six months had elapsed between the time when the details of the plan of study were worked out and the time of its final adoption. The disaster at Pearl Harbor occurred before the work was started and apparently many of the participating investigators were persuaded to alter the proposed plan of study because of the report of observers who had returned from Hawaii. The latter had been profoundly impressed by the low incidence of wound infection, which they believed to have been due to the copious local application of sulfanilamide.

Not unnaturally, the judgment of these observers was greatly influenced by their enthusiasm and by the intensity of the dramatic aspects of their brief experience. Subsequently, more careful and deliberate observations apparently bore out the suspicion of many of the responsible investigators that the enthusiasm was not warranted or, at least, was premature and somewhat excessive. Fortunately, the scientific integrity of all the participants was beyond question, and the enthusiasm rapidly gave way to the tempered and deliberate judgment of the more conservative investigators.

The final results seemed to have justified this conservative attitude. The subsequent studies brought out many of the vital factors concerned in the development and persistence of infection in wounds and burns. The sulfonamides, used systemically, were found to minimize the general spread of infection and to cut down the incidence of sep-

ticemia and death. There was no evidence, however, that these drugs, with the methods employed—local, systemic or both,—produced any significant reduction in the incidence of local infection in the wounds. Thus, the report concludes, "we are going to lessen the incidence of local infections in war wounds and burns, some other form of the sulfonamides or some other bacteriostatic agents must be found which will be effective against the contaminating organisms in the presence of damaged tissue."

Since penicillin is active in the presence of damaged tissue, and, in effective amounts, is apparently not toxic to healthy tissues, this agent naturally presents itself as a possible logical answer to some of the objections raised in the report. Comment has already been made in this column concerning the experience of British investigators in England and in the Mediterranean area.² The concrete and practical results of these and other studies are now available in the form of a memorandum issued by the Medical Research Council.³ This memorandum gives the instructions prepared by the Penicillin Clinical Trials Committee for the use of penicillin in war wounds.

Studies on the use of penicillin in surgical infections in Army camps were reported by Lyons⁴ last winter. His report confirms the usefulness of penicillin in the treatment of wounds, even after they have become established, but he aptly emphasizes its role as a supplement in the overall surgical management of cases. He points out how the effectiveness of penicillin in controlling infection has aided the rapid re-establishment of a positive nitrogen balance, thus permitting the regeneration of hemoglobin and red cells in gunshot and other deep wounds. As in most similar therapeutic studies, the patients concerned probably received better and more skillful general care and attention than are afforded the average case with the same type of lesions. This must always be borne in mind in evaluating the merits of any agent or procedure.

The difficulties of evaluating drug treatment in surgical infections have recently been reviewed by Meleney,⁵ an investigator whose extensive studies in the field make him particularly well qualified to discuss this subject. He points out the numerous

persons involved in surgical infections, in contrast to those in other infectious diseases or what he calls "medical infections." The importance of weighing and measuring all these factors makes the appraisal of drugs in surgical infections infinitely more difficult than it is in most medical infections, and these difficulties apparently apply to penicillin as well as to the sulfonamide drugs.

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CORRESPONDENCE

CIVILIAN NEEDS FOR WHOLE-BLOOD TRANSFUSION

To the Editor: Emergency situations when a blood transfusion is needed without delay have a way of occurring regardless of time, traffic or the vagaries of New England weather. Despite the stopgap that commercially available plasma fluids, the war has emphasized the superiority of whole blood. Yet often hours pass before even donors of known types are cross matched and the blood administered. Hemorrhage is just as serious in a civilian automobile casualty or a new mother as it is in a serviceman.

Is it not high time to utilize public interest and good will in saving the life of a neighbor in the postwar world? Even he's self, one's wife or one's child may be the victim.

All servicemen have been typed. Most civilians are anxious to know their own blood types. They are anxious to donate to blood banks since learning that they need fear no effects. If physicians can organize the activities, the people have shown they will co-operate. Local community donor lists at least could easily be arranged.

We now have the techniques, equipment and trained personnel in the large Boston hospitals. The small hospitals should have access to the services of state, municipal or Red Cross supported centers with twenty-four-hour telephone and motor-transport service for blood, plasma or donors available to all doctors on request. Patients could be charged according to their incomes.

Central blood-collecting and typing centers in Boston, Worcester and Springfield need but the stimulus of the Massachusetts Medical Society to portray the need by press and radio.

No one knows how long the war will last. It is not, however, too early to plan to prevent needless loss of life on the home front now.

JOSEPH B. DOYLE
 Lieutenant Commander (MC), U.S.N.R.

EMIC PROGRAM

To the Editor: I have just read your editorial in the September 7 issue of the *Journal* entitled "Massachusetts EMIC Program" and because to me it appears that there are perhaps some phases of this program that you do not fully understand I am taking the liberty of writing to you about this matter.

While I am agreed that it is desirable to free from worry the men in the armed service regarding the proper care of

their family, — provided that these men are subject to worry because of financial handicaps, — I cannot agree that the method chosen is either wise or proper. Many of the men in the lower four pay grades are amply able to provide adequate medical care for their wives. However, if it be argued that all of these men should be treated alike, regardless of financial status, then we would contend that each be given a definite sum of money for such care, the amount to be fixed by Congress, and that these men then be permitted to expend this money for service as they elect.

Some may want hospital care and a private nurse and a specialist to attend the wife, some may want a home delivery by the family doctor, and still others may want ward care in the hospital. In either case they would be able to elect the type of care that best suits their condition, whereas under EMIC each must accept ward care in a hospital and a doctor whose fee does not deter him from accepting such cases. And if a doctor cannot be induced to sign up for the case, then hospitalization is not available.

This plan would avoid the regimentation of the doctors, which to us is the most objectionable feature of the EMIC program.

I would also respectfully call your attention to the statement "according to the Children's Bureau, it will terminate six months after the war is ended." In fact this means that no new cases will be signed up after six months after the war is ended, but all cases signed up prior to this time will be carried to completion, and since the program provides care for the mother for six weeks after the delivery, and care of the infant for one year after birth it will be seen that the program will not end for more than two years after the end of the war.

Your attention is also directed to the new regulations of the Children's Bureau, which provide that after a doctor has signed up to care for an expectant mother he is thereby obligated to render to her every service that can be rendered in his office, regardless of whether or not it be connected with pregnancy. And the pay for all of this service is included in the one fee which he may collect. To take an extreme case, but one which might well occur: A doctor signs up to provide care for an expectant mother and during the pregnancy she suffers a fractured humerus, or similar accident, which he treats. She later goes to another city where she is delivered. The doctor who gave her the prenatal care may collect a maximum of fifteen dollars for prenatal care, including the care of the fractured humerus, provided she made seven visits to his office for prenatal care. If she made less than seven visits he must deduct two dollars for each office visit less than seven, and this without regard to her ability to pay for medical care.

This EMIC program has received rather close study by the Maternal and Child Health Committee of the Nebraska State Medical Society, of which committee I happen to be a member, and our committee has not enthused about the provisions of the program at any time, and are perhaps less enthusiastic about it since the promulgation of the new rules. Nor have many of the Nebraska physicians enthused about the program when they understood it.

It is our experience that the most ardent supporters of the program are those who have least understood it, whereas those who have given it close study almost universally feel that it is simply a foot in the door for state medicine.

In closing may I say that this letter is not meant to be critical of the *Journal* or its editorial staff. I have a very high regard for the *Journal* as evidenced by my being a subscriber for more than twenty-five years, but it is simply intended to explain why some doctors do not approve of the EMIC program and why they fear the influence of the Children's Bureau as the personnel is now constituted.

In determining whether or not this is a good type of medical care "as a steady diet" I feel that the paramount issue is whether or not it is a good thing for the sick patient. If we should decide that it is, we should lend our support to its extension; if we believe that it is not, then we should try to educate the public to its dangers and shortcomings, because in the final analysis whatever is good for the man who is ill, regardless of its effect on the doctor or the politician, is the type of medical care toward which we must aim if we are to do our full duty to posterity.

I hope that I have made clear my position with regard to the EMIC program. I have no criticism for those whose views may differ from mine.

G. E. PETERS

Randolph, Nebraska

The following resolutions were adopted at a meeting of the American Pediatric Society, held in Atlantic City, New Jersey, on September 26:

Whereas the objectives of the American Pediatric Society and those of the Children's Bureau concern the betterment of the health and welfare of the children of America, any break in the hitherto good relation of the two organizations would be harmful to the ends desired.

Whereas cash grants under the EMIC program would negate one of its principal purposes and would establish a dangerous precedent, and whereas all medical care for mothers and children under the Social Security Act, Title V, was designated in 1935 by Congress to be given on a service basis rather than as cash grants, a change in the method of payment in the EMIC program is not warranted or desirable.

Whereas the Miller Bill, now before Congress, advocates the transfer of the Health Services of the Children's Bureau to the United States Public Health Service, and in so doing would separate medical care from the other essential aspects of child care, and whereas the Miller Bill does not make any provision for the development of a National Department of Health, the American Pediatric Society feels that the transfer advocated in the bill is undesirable.

Whereas it is desirable to assemble facts and develop considered opinions on postwar planning for children before the meeting of the American Academy of Pediatrics in November, the American Pediatric Society requests that the American Academy of Pediatrics authorize its special committee on the EMIC program or another specially appointed committee to confer with a committee of three appointed by the American Pediatric Society and three members of the Medical Advisory Committee of the Children's Bureau and that this joint committee submit a report to the American Academy of Pediatrics at its November meeting.

Since these resolutions were adopted by a group whose members are well acquainted with the EMIC program, they serve to refute certain of the arguments raised in Dr. Peters's letter. — Ed.

DEPRIVATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held September 13, the Board voted to revoke the license to practice medicine of Dr. Mary E. Bolger, 442 Cambridge Street, Worcester, because of the violation of her probationary period as of February 10, 1942.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

To the Editor: At a meeting of the Board of Registration in Medicine held September 13, the Board voted to revoke the license to practice medicine of Dr. Don D. Cornell, American Hospital, Picher, Oklahoma, because of the violation of the Narcotic Act.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Backache and Sciatic Neuritis: Back injuries — deformities — diseases — disabilities. By Philip Lewin, M.D. Line drawings by Harold Laufman, M.D. 8°, cloth, 745 pp., with 235 illustrations. Philadelphia: Lea and Febiger, 1943. \$10.00.

This book was written expressly to familiarize general practitioners with the problem of back pain. It can be said that the subject has been covered from the standpoint of terminology and that the text also includes most of the described syndromes known to the profuse literature on backache. Since there exist differences of opinion among authorities and since empiricism holds sway over scientific evi-

dence, the subject is difficult, but is fairly dealt with by the author. On the other hand, because the information in the book is a maze of generalities, the practitioner, although aware of more facts, is none the better prepared to reach a conclusion in a given case, either concerning diagnosis or treatment. Analysis of a given case is the keynote throughout yet no basis for the analysis is given; instead, the reader is many expressed viewpoints without critical reasoning to judge the good from the bad and is therefore apt to be left confused rather than clarified. On the whole, the book represents a tremendous amount of time in preparation, and the reviewer believes that the most valuable contribution is its extensive bibliography.

The Arthropathies: A handbook of roentgen diagnosis. Alfred A. de Lorimier, M.D. 8°, cloth, 319 pp., with 171 illustrations. Chicago: The Year Book Publishers, Incorporated, 1943. \$5.50.

The clinical and grosser roentgen features of the arthropathies are presented in usable tabulated form, abundantly illustrated by negative prints. This should be helpful to medical students, general practitioners and those whose diagnostic method is more clinical than roentgenologic.

The factual presentation is accurate, but caution may be advised in considering the theoretical explanations of the facts. The section on the spine falls below the standards attained elsewhere in the book.

The conditions included under the various group diagnoses are not synonymous, although they are listed under the heading "synonyms."

The meaning of the descriptive terms is not always entirely clear and the terms are rather broad in their application. For this reason the list of roentgenologic features for one diagnostic group may appear similar to those for another group.

The illustrations have been made from good films, but much detail has been lost in reproduction.

Medical Parasitology and Zoology. By Ralph W. Naus, M.D., Dr.P.H. With a foreword by John C. Torrey, Ph.D. 8°, cloth, 534 pp., with 95 illustrations and 15 tables. New York: Paul B. Hoeber, Incorporated. 1944. \$6.00.

The subject matter of this book is divided into four parts: the first of which deals with protozoa parasitic in man, the second with worms parasitic in man, the third with arthropods and disease transmission, and the fourth with poisonous and venomous animal life, including insects, coelenterates, mollusks, fishes, biting water bugs, snakes and lizards. In addition, the appendices contain valuable sections on the care and use of the microscope, methods for study and diagnosis of parasitic infections and summaries of the distribution and numbers of species of elapid and viperid venomous snakes of the nearctic and neotropical regions. The glossary includes a classification of animal parasites and arthropods and a helpful section of pertinent definitions. A bibliography and a subject index are provided.

The parasites are usually discussed under headings of geographical distribution, morphology, life cycle, epidemiology, pathology, symptomatology, diagnosis, treatment and prophylaxis. The bionomics and epidemiologic aspects of the more important species are not adequately dealt with to meet the needs of either student or practitioner, and seemingly contradictory statements will probably create some confusion. For example, on page 179 the reader is led to believe that the miracidium of *Clonorchis sinensis* does not hatch outside the molluscan host. On the following page, however, hatching of this miracidium is graphically illustrated in Figure 45, and it is stated, "In water it escapes through the opercular end of the egg to seek a suitable snail host."

The names *Oxyuris* and *Trichocephalus* are listed in the glossary as synonyms of *Enterobius* and *Trichuris*. The manner in which they are cited, however, *Enterobius (Oxyuris) vermicularis* (page 137) and *Trichuris (Trichocephalus) trichiura* (page 141) brings them into subgeneric rank, according to the International Code of Zoological Nomenclature.

The verbal descriptions of important parasites, particularly of the parasitic protozoa, and the tabular data on differential diagnoses are well done, with the desired information made readily available. Unfortunately, Figure 2 (gran-

entiation of amebae) is poorly executed and gives an erroneous conception as to the relative size of the species illustrated.

The book has greater value as a laboratory aid than as a text. The format is pleasing.

BOOKS RECEIVED

The receipt of the following books is acknowledged, this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Birth Without Fear: The principles and practice of natural childbirth. By Grantly Dick Read, M.D. (Camb.). Cloth, 259 pp. New York and London: Harper and Brothers, 1944. \$2.75.

This manual has been written primarily for expectant mothers. It advocates education and preparation during months of pregnancy, with the belief that the mind and body will be relaxed to an extent that will materially lessen discomforts of childbirth. The author believes that fear is the part of the expectant mother has much to do with during labor. The book discusses the anatomy, physiology and psychology of birth, emphasizing the emotional and mental aspects. It should prove interesting to physicians, nurses and psychologists, as well as to mothers.

Textbook of Dermatology. By Norman Tobias, M.D., senior instructor in dermatology, St. Louis University, assistant dermatologist, Firmin Desloge and St. Mary's Hospitals, visiting dermatologist, St. Louis City Sanitarium and St. Louis Hospital. Second edition. 12°, cloth, 497 pp., with 110 illustrations. Philadelphia: J. B. Lippincott Company, 1944. \$4.75.

The second edition of this manual, first published in 1941, has been revised and brought up to date, still keeping the scope of the book within its original limits. The latest accepted treatments are described and the obsolete ones have been deleted. Brief descriptions of the rare dermatoses are included in this edition for the sake of completeness.

Textbook of Nutrition. A symposium prepared under the auspices of the Council on Foods and Nutrition of the American Medical Association. 8°, cloth, 586 pp. Chicago: American Medical Association, 1943. \$2.50.

This is a collection of papers on various aspects of nutrition specialists in their particular fields.

Arthus's Philosophy of Scientific Investigations: Facet de l'aphylaxie à l'immunité Paris (1921). Translated from the French, with an introduction, by Henry Sigerist, M.D., foreword by Warfield T. Longcope, M.D. Cloth, 26 pp. Baltimore: The Johns Hopkins Press, 1943. 75 cents.

This translation of a historically important article was first published in the October, 1943, issue of the *Bulletin of the History of Medicine*. It is now issued separately in bound form. It originally preceded the text of Arthus's book on aphylaxis and immunity. It was addressed to the author's physician and is a bit of medical literature that is worthy of being preserved and should be in all medical and scientific libraries. In its own way it compares favorably with the celebrated introduction to the study of experimental medicine of Claude Bernard, although Arthus's article is limited to a comparatively few pages.

Occupational Lead Exposure and Lead Poisoning. A report prepared by the Committee on Lead Poisoning of the Industrial Hygiene Section of the American Public Health Association. 8°, paper, 67 pp. New York: American Public Health Association, 1943. 75 cents.

This is a timely up-to-date monograph on an important problem in industrial medicine. The first three parts have to do with industrial lead exposure, and therein are discussed the recognition of the hazard, the safe limits of exposure and the control of exposure. This is followed by a chapter on occupational lead poisoning, in which diagnosis is stressed and the various types are described. The monograph concludes with a short discussion on management and treat-

ment. A valuable bibliography on the subject is appended to the text.

Studies from The Rockefeller Institute for Medical Research. Reprints. Volume 124. 8°, paper, 626 pp., illustrated. New York: The Rockefeller Institute for Medical Research, 1943.

The Medical Clinics of North America: Cardiovascular and blood diseases. Chicago number: January, 1944. 8°, cloth, 289 pp., with 37 illustrations and 8 tables. Philadelphia and London: W. B. Saunders Company, 1944. \$3.00.

Intravenous Anesthesia. By R. Charles Adams, M.D., C.M., M.S. (anes.), associate in Section on Anesthesiology, Mayo Clinic, instructor in anesthesiology, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minnesota. 8°, cloth, 663 pp., with 75 illustrations. New York: Paul B. Hoeber, Incorporated, 1944. \$12.00.

This treatise comprises a comprehensive review of the use of intravenous anesthesia from its inception until the present time. All the available literature on the subject has been consulted. All the drugs that have been administered intravenously to produce anesthesia, as well as the various methods that have been employed and the results obtained from them, have also been reviewed. A chapter on intravenous anesthesia in military surgery closes the book.

Barometric Pressure: Researches in experimental physiology. By Paul Bert, M.D. Translated from the French by Mary Alice Hitchcock, M.A., and Fred A. Hitchcock, Ph.D., associate professor of physiology, Ohio State University. 8°, cloth, 1055 pp., with 89 illustrations, 23 tables and frontispiece. Columbus, Ohio: College Book Company, 1943. \$12.00.

In 1878, Dr. Bert published his classic text on the effects of barometric pressures on man. This translation is welcomed at this time when it can be of service to investigators in the field of aviation medicine. Dr. Bert was a pioneer in his field, and his work on the physiology of altitude is of much value today. His application of Dalton's concept of partial pressure to human respiration became the basis of all subsequent work in the field of altitude physiology. The original French edition is a scarce book, and the translators should be thanked for providing an English edition at this time.

Intracranial Arterial Aneurysms. By Walter E. Dandy, M.D., adjunct professor of surgery, Johns Hopkins University. 8°, cloth, 147 pp., with 55 illustrations and 7 charts. Ithaca, New York: Comstock Publishing Company, Incorporated, 1944. \$2.50.

This special monograph reflects the experience of the author in the diagnosis and surgical treatment of intracranial arterial aneurysms, with a record of 20 cured patients. The work is well illustrated and detailed charts containing complete information are appended to the text. There are 37 cases of aneurysms of the internal carotid artery, 25 of the anterior cerebral and anterior communicating arteries, 22 of the middle cerebral artery, 2 of the posterior cerebral artery, and 21 of the vertebral and basilar arteries. There is also an extensive bibliography.

The Management of Neurosyphilis. By Bernard Dattner, M.D., Jur.D., associate clinical professor of neurology, New York University Medical College. With the collaboration of Evan W. Thomas, M.D., assistant professor of medicine and assistant professor of dermatology and syphilology, New York University Medical College; and Gertrude Wexler, M.D., instructor in dermatology and syphilology, New York University Medical College. With a foreword by Joseph E. Moore, M.D., associate professor of medicine and adjunct professor of public health administration, Johns Hopkins University, physician-in-charge, Syphilis Division, Medical Clinic, and visiting physician, Johns Hopkins Hospital, Baltimore, and special consultant, United States Public Health Service. 8°, cloth, 398 pp., with 7 illustrations, 27 tables and 4 charts. New York: Grune and Stratton, 1944. \$5.50.

This special work is based on an experience of more than twenty years in dealing with neurosyphilis in its many aspects. The plan adopted in this work is similar to that used by the author in a similar book, written in Vienna in 1933. The work is divided into two parts: the first on the examination, the interpretation and the evaluation of the spinal fluid; and the second on methods of treatment. A comprehensive bibliography is attached to the text.

Harofé Haiori: Symposium on war medicine. In two volumes. Edited by Moses Einhorn, M.D. 8°, paper; Vol. I, 238 pp., and Vol. II, 223 pp., illustrated. New York: The Hebrew Medical Journal, 1943.

In these two volumes are included a number of articles on the surgical aspects of war medicine. In addition there are three articles on Palestine and the war. A 20-page dictionary of medical terms in Hebrew and English appears in Volume II. The text is printed in Hebrew and English.

Tuberculosis of the Ear, Nose and Throat: Including the larynx, the trachea and the bronchi. By Mervin C. Myerson, M.D., 8°, cloth, 291 pp., with 88 illustrations. Springfield, Illinois: Charles C Thomas, 1944. \$5.50.

This up-to-date manual is based on the personal experience of the author and is designed for the use of the otolaryngologist and bronchoscopist. Particular consideration has been given to tuberculosis of the larynx, trachea and the bronchi, where newer knowledge has been revealed by the bronchoscope. Diagnosis, prognosis and treatment are clearly described, based on the author's experience with over 10,000 tuberculous patients. The book is well printed on good paper, and well illustrated. Selected bibliographies are appended to each chapter.

On Growth and Form. By Sir D'Arcy Wentworth Thompson. 8°, cloth, 1116 pp., with 555 illustrations and frontispiece. New York: Macmillan Company, 1943. \$12.50.

This reference book was first published in 1917 during World War I and quickly went out of print. It has been carefully revised, reset, and considerably enlarged, giving the author solace and occupation when he was debarred from war service by his age. The book deals with the biologic problems of growth and form, and form and function in their necessary relation to physical principles and mathematical laws. The treatment of this complicated subject is simple; the physics and mathematics are elementary but comprehensive enough to throw light on fundamental problems of biology. This treatise on its subjects takes in material in botany, zoology, cytology, anthropology, mathematics, physics, chemistry, engineering, psychology and aesthetics.

Civilization and Disease. By Henry E. Sigerist, M.D., D Litt., LL.D., William H. Welch Professor of the History of Medicine, Johns Hopkins University. 8°, cloth, 255 pp., with 52 illustrations. Ithaca, New York: Cornell University Press, 1943. \$3.75.

In this book Dr. Sigerist has traced the varied and multiple influence of disease on every aspect of civilization. The work is based on a series of six Messenger Lectures, delivered at Cornell University in 1940, and expanded into a volume of twelve chapters. The first chapter on civilization as a factor in the genesis of disease is followed by chapters on disease and its relation to economics, social life, law, history, religion, philosophy, science, literature, art and music. In the final chapter, "Civilization against Disease," the author briefly reviews the advance of public health and its prospects for the future.

Studies from The Rockefeller Institute for Medical Research. Reprints. Volume 125. 4°, paper, 607 pp., illustrated. New York: The Rockefeller Institute for Medical Research, 1944.

Medical Diagnosis: Applied physical diagnosis. Edited by Roscoe L. Pullen, M.D., instructor in medicine, Tulane University of Louisiana School of Medicine, and assistant clinical director, Charity Hospital of Louisiana at New Orleans. With a foreword by John H. Musser, M.D., professor of medicine, Tulane University of Louisiana School of Medicine, and senior visiting physician, Charity Hospital of Louisiana at New Orleans. 8°, cloth, 1106 pp., with 584 illustrations and 12 colored plates. Philadelphia and London: W. B. Saunders Company, 1944. \$10.00.

This new work on medical diagnosis has been written on the premise that the scope of the subject has undergone sweeping changes and that for this reason a new work is justified. The author advocates complete examination of a sick person rather than a partial scrutiny of special symptoms and conditions. The work is divided into two parts, the first concerns the principles of physical examination, containing the procedures for examination of the patient as a whole. The second

has to do with special examinations, and here will be found chapters on psychosomatic medicine, mental measurements, electroencephalography, physical diagnosis of children, sterility surveys, occupational injury and military problems.

NOTICES

NATIONAL COMMITTEE FOR MENTAL HYGIENE

The thirty-fifth annual meeting of the National Committee for Mental Hygiene will be held on November 8 and 9 at the Hotel Pennsylvania in New York City. The decision to have a two-day annual meeting this year was prompted by the unusual opportunity and challenge to mental hygiene inherent in war activities, and in reconstruction and rehabilitation after the war. Topics for the various sessions will include the following: "Mental Hygiene of Industry and Reconversion"; "Rehabilitation and the Returning Veteran"; "Race Relations"; and "Services to the Mentally Ill Today." Various aspects of these topics will be discussed by persons of experience and influence in the various fields, and at each session about half the time will be reserved for discussion from the floor.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 26

FRIDAY, OCTOBER 27

The Diagnostic Significance of Changes in the Appearance of the Tongue Dr. H. J. Jeghers Joseph H Pratt Diagnostic Hospital

SATURDAY, OCTOBER 28

*10 00 a m -12 00 m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, OCTOBER 30

12 00 m -1 00 p m Clinicopathological conference Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 31

*12 15 -1 15 p m Clinicoroentgenological conference Peter Bent Brigham Hospital

WEDNESDAY, NOVEMBER 1

*12 00 m. Clinicopathological conference Children's Hospital

*Open to the medical profession

OCTOBER 25. Graduate seminar in pediatrics Children's Medical Service, Massachusetts General Hospital, Amphitheatre 3A. 7 15 p m

OCTOBER 30 New York Institute of Clinical Oral Pathology, New York Academy of Medicine Page 110, issue of July 20.

NOVEMBER 2-4. Association of Military Surgeons. Page xiii, 1944 of August 17.

NOVEMBER 8 and 9. National Committee for Mental Hygiene. Not elsewhere on this page.

NOVEMBER 9. The Clinical and Roentgenological Diagnosis of Carcinoma of the Lung. Dr. Merrill Sosman. Pentucket Association of Physicians 8 30 p m, Haverhill

NOVEMBER 15. New England Oto-Laryngological Society. Page 50 issue of October 5.

DECEMBER 13 and JANUARY 3 TO APRIL 25 Metropolitan State Hospital Page 508, issue of October 5.

FEBRUARY 19. American Board of Internal Medicine Page 436, 1944 of September 21.

DISTRICT MEDICAL SOCIETIES

PLYMOUTH

OCTOBER 19 Moore Hospital, Brockton
NOVEMBER 16 Plymouth County Hospital, South Hanson
JANUARY 18 Brockton Hospital, Brockton
FEBRUARY 15 Jordan Hospital, Plymouth
MARCH 15 Goddard Hospital, Brockton
APRIL 26 Toll House, Whitman
MAY 17. Lakeville Sanatorium, Lakeville
All meetings will be held at 11 a m

SUFFOLK

DECEMBER 7. Censors' meeting

WORCESTER

NOVEMBER 8 Grafton State Hospital
DECEMBER 13 Worcester City Hospital
JANUARY 10 St. Vincent Hospital, Worcester
FEBRUARY 14 Worcester State Hospital
MARCH 14. Worcester Memorial Hospital
APRIL 11 Hahnemann Hospital, Worcester
MAY 9 Annual meeting

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STUDIES IN MEDICAL SOCIOLOGY

II. The Relation of Mental Disorders to Population Density

MAJOR ROBERT W. HYDE, M.C., A.U.S., AND SERGEANT LOWELL V. KINGSLEY, A.U.S.

BOSTON

IN THE preceding study showing the relation of mental disorders to community socioeconomic level, variations in the rates of certain mental disorders were attributed to differences in population density. The purpose of the present study is to show these variations and to present possible explanations. Although there has been extensive investigation of rural-urban differences,^{1, 2} there has been no psychiatric study of an unselected cross section of the population. Previous work has usually been based on mental-hospital admissions and delinquency rates. Studies of this type do not eliminate the selective factor involved in local differences in attitude toward hospitalization and law enforcement.

Another weakness of rural and urban studies is the failure to make any correction in the findings for differences in socioeconomic level; hence, it has been difficult to isolate the rural-urban differences that are due to the differences in population density per se and not to the differences in economic level.

The examination of men coming to the Boston Armed Forces Induction Station from both rural and urban communities offers an excellent opportunity for the study of an unselected group of the male population. The communities sending selectees here have been classified regarding index of socioeconomic level according to grades of desirability, explained in more detail in other studies.^{3, 4} Since the relation of mental disorders to desirability level has been demonstrated,⁴ it is possible to make a correction for that factor and hence to approach the relation between mental disorders and population density.

One of the most significant studies of the relation of mental disorders to population density is that of Dayton,⁵ who found that, although 7.6 per cent of the population of Massachusetts is rural, only 3.9 per cent of first hospital admissions for mental diseases in Massachusetts were from rural environments. Mental disorders in patients from

rural environment were largely those associated with physical conditions, — namely, senile psychoses, mental deficiency, Huntington's chorea, somatic disease and arteriosclerosis, — whereas the most frequent abnormalities from the urban communities were paranoia, manic-depressive psychoses and psychoneurosis.

Shaw et al.⁶ found that delinquency rates dropped rapidly from the densest center of Chicago toward the least dense periphery, regardless of the nationality at the center, and like findings have been shown for Boston by the Boston Council of Social Agencies.⁷ In the examination of men drafted in World War I, mental deficiency was seen to be highest in rural areas, and other mental and nervous disorders and chronic alcoholism were higher in urban areas.⁸ These latter findings, although highly significant, are based on a far less extensive psychiatric examination than that done for the induction of men into the armed forces in World War II.

METHOD OF STUDY

The present study considers the same men as did that of the previous study of socioeconomic level, namely, those selectees from the eastern segment of Massachusetts examined at the Boston Induction Station during the winter, spring and summer months of 1941 and 1942.

The area includes a population distribution that is densest in Boston and includes 4 other cities of over 100,000 population, 5 with more than 50,000, 9 with more than 25,000 and over 50 towns and villages each with a population less than 2000. The sparsely populated areas represented are those of Cape Cod, the region inland from the southern coastal cities of New Bedford and Fall River and the region above the large cities immediately north of Boston.

Although the population is predominantly urban, the rural population is sufficient to be of significance. It is difficult to obtain any greater diversity of population densities than is present here and at

the same time to have all selectees examined at the same induction station, by the same criteria and by the same team of examiners. Because of the uniformity of the examinations on which the present study is based, it is possible to avoid the criticism made in connection with the World War I study of rural-urban comparisons that a large part of the differences is probably due to the more critical examinations made by the physical examiners in the large cities.⁹

Although the rating of density according to population per square mile does not always indicate the extent of overcrowding because of the occasional presence of densely populated and sparsely populated areas within the same community, it serves the purpose of a community study of this type. A more intensive study of density would take into consideration the average number of people per room and the proportion of uninhabitable land in any area.

In order to interpret properly the significance of our findings on the relation of mental disorders to population density, several factors related to density will be mentioned in the course of the explanation so that findings more closely associated with these related factors will not be falsely attributed to density. These factors are socioeconomic level, national origin, gravitation and ascent, selective migration and heredity.

Socioeconomic level has previously been shown to have considerable influence on the rate of psychiatric disorders. In the previous study all communities were rated according to medical, educational and recreational facilities, "class," public works, housing and welfare rates, and grouped into six categories of desirability, with A the rating for the best communities and F that for the poorest.

The *national origin* of people in a community, as shown by the proportion of people from certain nationalities, seems sufficient to account for variations in rates of mental disorders. There is considerable difference in distribution, with the Irish, Italians and Russian Jews the major elements in some of the large cities and French Canadians and Portuguese in others, with higher proportions of Old Americans in many of the suburban and semirural areas.

There is *gravitation* of the inadequate to the poorer communities and *ascent* of the ablest into the better communities.

Selective migration is that of the adventurous rural youth to urban areas.

Heredity is a difficult factor to measure, but is closely allied with density because of the fact that marital choice is more limited in areas of lower density and increases the chances of inbreeding.

This paper deals primarily with the effect on mental disorder of the cultural factors related to popula-

tion density. The aim is not to depreciate biologic factors, but to simplify the explanation of the findings and to discover how extensively cultural explanations are applicable. To do this the following hypothesis has been adopted: mental disorders in any community are to a great extent determined, both in type and in prevalence, by the culture of the community. The amount and types of mental stress and the acceptability of both normal and abnormal outlets from stress are parts of the culture and determine the type of disorder manifested.

The hypothesis presented by Faris and Dunham¹⁰ that communication is essential for normal mental development and that social isolation makes for mental breakdown appears to be especially pertinent to these findings.

RESULTS

In Table 1 the rates for all major causes of psychiatric rejection are related to different population densities. The rates for all communities with a population density of over 500 per square mile show a steplike increase in mental disorders from 7.5 up to 14.0 per cent with increased population

TABLE 1. *Relation of Percentage Rejected for All Major Psychiatric Causes to Community Density of Population.*

DENSITY PER SQUARE MILE	No. EXAMINED	REJECTION RATE	SOCIOECONOMIC LEVEL
		%	
Less than 500	2,856	12.1	D+
501-999	4,478	7.5	B-
1000-1999	6,340	8.5	C+
2000-4999	8,056	9.2	C
5000-9999	13,322	9.5	C
10,000-19,999	14,108	10.6	D
20,000 or over	10,840	14.0	E

density. The communities of less than 500 people per square mile stand out markedly from this pattern with the high rate of 12.1 per cent. This table indicates that to a considerable extent the relation to density of the total rate of psychiatric rejection can be explained on the basis of variation in socioeconomic levels. Only in the consideration of those communities that present rates for mental disorder varying from that to be expected on the basis of socioeconomic level, and in that of specific mental disorders, is the importance of population density alone demonstrated. Each of the communities of density of less than 500 per square mile was investigated, and some presented an unexpected deviation from the average rate for that density level. The three communities that had especially high rates included isolated areas and appeared to represent the features of degenerate rural communities in which the ill effects of isolation and of inbreeding may exist.

A study was made of the communities that had the highest rates of mental disorders and those that

the lowest. Of the 13 communities with extremely high rates, 8 were in the extreme density bracket (over 20,000 people per square mile). By contrast, of the 13 communities with extremely low rates, not one was in either extreme density bracket (under 500 or over 20,000 population density). Ten of the 13 were in areas characterized by one-family or two-family houses and 9 were in suburbs of Boston.

In order to define the interrelation of socioeconomic status and population density, the socioeconomic level was determined of those communities in each density level that varied in rate of mental disorders from the average rate of the group as a whole. Twelve of the 14 communities with low rates for mental disorders were of a higher socioeconomic level than that of the density group to which they belonged, confirming the influence of socioeconomic level within the same population density. A similar study was made of differences in population density of communities in each socioeconomic level whose rates varied from the group average. Those communities with populations of less than 500 and over 20,000 per square mile tended to have higher rates than the group average.

Although the total psychiatric rejection rate does not reveal the extent to which differences in rate can be directly attributed to density of population, it is apparent when the separate causes of rejection are examined that change in type of disorder rather than in amount of disorder is notable in different density levels.

Mental Deficiency

The relation of mental deficiency to population density is represented in Table 2. An outstanding finding is that throughout the entire intermediate range of density from 500 up to 20,000 per square mile there was no significant difference in the rate of mental deficiency. The highest rate was found in

TABLE 2. *Relation of Percentage Rejected for Mental Deficiency to Community Density of Population.*

DENSITY PER SQUARE MILE	REJECTION RATE
	%
Less than 500	2.7
500-999	1.3
1000-1999	1.5
2000-4999	1.6
5000-9999	1.3
10,000-19,999	1.2
20,000 or over	2.2

in communities of population density less than 500 per square mile, and the next highest in those of population density at the other extreme, over 20,000 per square mile. The highest rate of mental deficiency in the rural areas confirms the findings of the studies of the draftees of World War I⁸ and that of Dayton.⁵

It is interesting to compare those communities having the highest rates of mental deficiency with

those having the lowest. All but 3 of the 11 communities with high rates of mental deficiency have predominant foreign elements, usually Italian and Portuguese. The relation of mental deficiency to nationality is significant and will be considered in a following paper.¹¹ The 3 other communities with high rates were rural communities having a predominantly Old American population. Each of these communities is known to contain areas of degeneracy and inbreeding. In one there is a neighborhood of albinos. Another includes islands wherein there are large numbers of deaf-mutes whose defects resulted from inbreeding, a fact described by Rosenau.¹² A third has many isolated areas. All these communities have a minority Portuguese population who live in their own settlements among the Old Americans. The high rate among the Portuguese for failure to meet the usual standards is one reason for the high rates found in these communities.

The degree of isolation of the 3 rural communities was further studied by examination of town reports to see to what extent townspeople married outside their community. It was found that they married within their neighborhood to a far greater extent than in other areas.

None of those communities with extremely low rates for mental deficiency were semirural (under 500 people per square mile), and none were dense urban communities (over 20,000 per square mile). The only communities with density over 10,000 per square mile were composed largely of Irish and Jews, who have a low rate for mental deficiency. The communities are all in Boston or suburban or adjacent to it.

Determination of the differences in mental deficiency in communities of different density but of the same socioeconomic level revealed a trend toward decreased rates of mental deficiency with increase of population density.

For an explanation one can first consider that suggested by Dayton⁵; namely, mental defectives tend to drift to the areas of lesser competition that are the least dense areas. To this could be added that the mental defectives originating in the rural areas are likelier to remain there and not to escape to the city, and that inbreeding occurs sufficiently often in certain isolated neighborhoods of these rural communities so that mental deficiency may be increased genetically. It is also likely that the decrease in mental stimuli in the simple rural cultures tends to increase the rates for failure to meet mental tests. Selectees having a rural background are apparently less frequently confronted with situations requiring the concentration and speed needed in an adequate test performance. As a result, they adapt themselves to the test situation less readily than do the urban selectees.

Gillette¹ states that illiteracy is four times as high in rural areas as in urban areas. It is known not

only that urban educational facilities are better, but also that the urban child's school attendance receives more social encouragement and statutory enforcement than does the rural child's. Although our tests are supposed to minimize the influence of education and literacy, it cannot be expected that this aim has been achieved in every case. People who have attended school are able to adjust themselves more quickly than others to the test situation.

Although the relation of mental deficiency to population density is concealed in part by its relation to both socioeconomic level and nationality, it may be concluded that in isolated rural communities there is an increase in the rate of mental deficiency, and that in urban communities, except in the slum areas of foreign population, there is generally a decrease.

Psychopathic Personality

The relation of psychopathic disorders to population density is represented in Table 3. The rate for psychopathic personality is high in rural communities, but the highest rate is in the densest communities. The relation of psychopathic personality to population density is less consistent than it is to socioeconomic level. The findings are notable, however, since previous studies of rates of delinquency, the disorder that compares most closely with our classification of psychopathic personality, have not

TABLE 3. *Relation of Percentage Rejected for Psychopathic Personality to Community Density of Population.*

DENSITY PER SQUARE MILE	REJECTION RATE
	%
Less than 500	3.5
500-999	2.2
1000-1999	3.2
2000-4999	2.8
5000-9999	3.4
10,000-19,999	3.5
20,000 or over	5.7

shown a high rural rate. In view of the fact that the country youth with criminal inclinations tends to migrate to the city to find richer fields for his crimes and a more adventurous existence, it is interesting that there is still a high rate of psychopathic personality in the rural areas.

Two of the low-density communities that had high rates for psychopathic personality also had unusually high rates for mental deficiency and were known to include degenerate areas. One other community with a high rate for psychopathy was of higher population density (1000-1999), but also included at least one community of degenerate Old Americans.

Conflicting factors enter into the rural rates for psychiatric disorders, for in the rural areas both work and play tend to be on a physical level, a circumstance that tends to increase physical outlets for asocial tendencies. On the other hand, asocial

conduct tends to be minimized by the strong social pressure of the family and neighborhood group that is so strong in the rural areas.

Since America has become urbanized with the coming of the industrial era, some rural disorganization has occurred, especially in the last three decades. The wage scale of rural life, even though it allows for security, does not always furnish the physical possessions — for instance, automobiles and movies, which have come to be part of American life. The home and group recreations of the rural community have given way to the commercialized recreations available in the neighboring cities. No longer is the rural youth content with simple rural pleasures. Since his desire for things is stimulated beyond his ability to satisfy it, he comes under the same social stress as does the boy in the slums. The ensuing disorganization is a result of a combination of economic and rural factors.

The extreme density of the urban slums is no doubt associated with their economic level in producing the high rate of psychopathic disorders. The sequence of circumstances may be that poverty tends to keep people in overcrowded slums, and that the overcrowding in turn throws them into too close contact with an abnormally large and diverse group of people. This increases the likelihood of gang development, of personal conflict and of association with older and more criminal associates.

Of those communities with the low rates for psychopathic personality none are of density over 10,000 per square mile and none are in Boston. It may be found with further study that the psychopathic personality of the city is not the same as that of the rural community. Possibly the urban type of psychopath is essentially an aggressive, acquisitive, asocial personality, whereas the rural psychopath is an irresponsible, futile and generally inadequate one.

Chronic Alcoholism

Table 4, showing the relation of chronic alcoholism to population density, reveals a totally different pattern than that of the previously considered mental disorders, for in the case of chronic alcoholism the rate in the rural communities (density less than 500) is not increased. There is a low rate in the 2 community groups of lowest density, and an increase with increasing population density. There appears to be a better correlation of chronic alcoholism with density than with socioeconomic level, for in the study of the latter it was shown that there was no appreciable difference in rates for chronic alcoholism between the communities in the upper segments of desirability (A, B and C communities).⁴

The strong relation of alcoholism to population density is further substantiated by an increase in alcoholism with the increasing density when a correction is made for economic level, and by the fact

that there are no low-density communities (density less than 2000 per square mile) that have a high rate of alcoholism, even though several have a low socioeconomic level.

The stimuli that help to promote drinking tend to increase in direct proportion to the density of the

TABLE 4. *Relation of Percentage Rejected for Chronic Alcoholism to Community Density of Population.*

DENSITY PER SQUARE MILE	REJECTION RATE %
Less than 500	0.6
500-999	0.6
1000-1999	0.8
2000-4999	1.1
5000-9999	1.2
10,000-19,999	1.4
20,000 or over	2.1

population. The farmer is not constantly confronted by whisky and wine advertisements and by bars and cafés. Not only stimuli but also opportunities are more frequently increased with density. Granted that the confirmed alcoholic addict will go far for a drink, somewhere in his development the matter of opportunity for frequent drinking must be important. The man who must pass a bar on every corner as he returns from work would be expected to drink oftener and more than if he had to go several miles to the nearest village to get a drink. Furthermore, the long working hours of the farmer and the time spent at sea by the fisherman decrease the frequency of their drinking.

The closer family life of the rural and semirural communities is conducive to more drinking at home and less in taverns and bars. To what extent this factor affects the incidence of alcoholism is not known, but it is quite possible that the man who drinks at home is favorably influenced by his wife and family to drink moderately, in contrast to the man in the tavern or at the bar, who is so often encouraged by his friends to drink to excess.

A further factor is that of the relation of drinking to sociability. In the rural areas, because of the lack of and need for gregarious living, there is a higher degree of sociability within the neighborhood whenever it is possible for people to get together. Because of the great congestion of the city, barriers are drawn up that isolate the individual from the crowd. In the urban settings the restraints of privacy that have become customs retard sociability, and alcohol serves to dissolve a man's restraint and to aid that freedom of social intercourse that occurs in the rural setting without its aid.

To emphasize density is not to minimize the other factors affecting alcoholism. There is an acknowledged gravitation of the alcoholic addict into a poorer community; there are nationalities with religious or ethical taboos against alcoholism, and there are others with excessive rates for alcoholism, a factor that will be shown in a following paper.¹¹

The question of acceptability of drinking is much disputed, and varies as much with local culture as does any other habit or custom, but in this consideration we point out only the importance of the relation to population density.

PSYCHONEUROSIS

Table 5, showing the relation of psychoneurosis to population density, reveals no consistent pattern. It is notable that the highest rate (4.9 per cent) occurs in the rural communities, with another peak of 4.2 per cent in the communities of 10,000-19,999 population per square mile.

In the relation of psychoneurosis to socioeconomic level, there are a decrease at the extremes and slightly higher rates throughout the communities of intermediate desirability. The finding of high rates in the rural communities is not in agreement with Dayton's⁵ finding of a higher rate of psychoneurosis in hospital admissions from urban communities. This appears to demonstrate the difference in find-

TABLE 5. *Relation of Percentage Rejected for Psychoneurosis to Community Density of Population.*

DENSITY PER SQUARE MILE	REJECTION RATE %
Less than 500	4.9
500-999	3.2
1000-1999	2.8
2000-4999	3.5
5000-9999	5.2
10,000-19,999	4.2
20,000 or over	5.7

ings between a cross-section study such as this one and a study involving the selective factors of hospitalization.

The finding of Sherman and Henry¹³ in *Hollow Folk* that the frequency of neuroses increased as the inhabitants moved from Colvin Hollow (an isolated backward community) to the outside world is not substantiated. It may be that the rural communities studied here present features of cultural disorganization and industrialization that are not present in the relatively backward and isolated Colvin Hollow.

A further factor that is probably important is the association of psychoneuroses with fear, ignorance and superstition that often occur in the isolated community. Medical attention, even when available, is in many neighborhoods infrequently sought, and when a man is in pain, he often listens to relatives and friends tell him what his trouble is or how they have seen someone die with just such a pain. Instead of going to a physician to obtain the reassurance of a diagnosis, he permits his fears to become so multiplied and aggravated that the apprehension and anxiety continue long after the pain is gone. Although competitive stress is not great in isolated rural areas, boredom often makes illness the most dramatic and interesting thing in

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The strong relation of alcoholism to population density is further substantiated by an increase in alcoholism with the increasing density when a correction is made for economic level, and by the fact

Rural communities are for the most part characterized by isolation, monotony of existence and lack of those commercialized recreations — theaters, soda fountains, bars and night clubs — that have come to be so demanded by urban society — and by lack of those business opportunities that modern civilization requires. Wages are adequate to buy those things considered necessary in rural culture — simple food, simple clothing and shelter — but not those things considered necessary in modern culture. Radios, automobiles, washing machines, flush toilets, vacuum cleaners and electric lights are difficult to obtain with rural wages. On the other hand, in the large cities, represented here by Boston, where the recreational facilities, business opportunities and modern conveniences that the rural areas lack are found, there are also the undesirable features of congestion and overcrowding, with the resultant lack of privacy, fresh air, open fields and woods. Commercialized recreation takes such a dominant place in urban life that home life is often weakened. The intensity of economic and social competition that overstimulates the individual may blunt his ethical sensitivity and make economic success his only important goal. The hopelessness of failure or the fear of it in such competition is as abject as the morbid discontent, apathy or boredom engendered in the rural areas.

Faris and Dunham¹⁰ find the factor of social isolation to be important in mental disorders in the densest urban rooming-house areas. Perhaps the anonymity afforded in the rooming-house area of the great city offers as great a degree of social isolation as do the rural areas, and perhaps the increased isolation in both these extremes of population density is responsible for the increase of rates of mental disorders at the extremes.

Only between these two extremes is there present the mean that satisfies most fully the aspirations of modern life. In the small city, and to a lesser extent in the moderate-sized city, there are those advantages of interest, stimulation, excitement of easily accessible recreational facilities, business opportunities and modern conveniences that are lacking in the rural communities, without the loss of the rural advantages of open fields, woods and strong family life. Security still exists to a great extent. The competition is not so intense as in the great city, aspirations are not so high, and the opportunities that are present are not overwhelming or confusing. The personality is not crushed by intense overcrowding and competition, nor is it stimulated to intensely aggressive action, as in the great city, nor stifled by isolation and boredom, as in the rural areas.

It is not surprising to find both the rural areas and the great city having similar rates for mental disorders, for both types of communities have many

unfavorable features. The most adequate people, as judged by their adaptation to modern life, migrate to the urban communities from both the rural and dense urban areas, leaving the less able people behind. Thus, the increased numbers of inadequate people left at the undesirable extremes of density, as well as unfavorable factors of these types of communities, account for the high psychiatric rates at the two extremes.

SUMMARY

The rejection rates for the major mental disorders found in selectees examined at the Boston Armed Forces Induction Station are compared with the population densities of the communities from which the selectees came, with the following findings.

Mental disorders differ in type in areas of different population density, irrespective of factors of socioeconomic level and national origin.

The highest rate of disorders are at the two extremes, with the highest rate of mental deficiency and psychoneurosis in the semirural areas and the lowest in the small cities.

The highest rate of chronic alcoholism and of psychopathic personality is in a large city (Boston); the lowest rate for chronic alcoholism in the semirural communities, and the lowest for psychopathic personalities in the small cities.

Only chronic alcoholism is correlated with population density throughout its complete range. It appears more closely associated with density than with socioeconomic level.

This study points to the need of intensive study in communities of different population density regarding the influence of the community environment on mental health.

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life. Births, deaths, accidents and operations are events of great social importance to the community, and as a result, neurotic manifestations are encouraged, especially among those who have few other ways of gaining attention.

COMMUNITIES OF A PREDOMINANT NATIONALITY BUT OF MARKEDLY DIFFERENT DENSITIES

Fortunately, the 4 communities that had the highest proportion of people of Italian origin represented an extremely wide range of density. They included at one extreme a mill town with outlying rural areas, and at the other, one of the world's most crowded slums. Their rates for major psychiatric disorders followed roughly the pattern of all communities arranged according to density (Table 6).

moderate-sized cities, and is exceeded only by the rate for a large city (Boston). Their rate for chronic alcoholism is lower than in the urban communities of all sizes.

Towns and small and moderate-sized cities. Cities of a great variety of size present similar patterns of rates for mental disorders. Even the pattern for large towns is similar to that in urban areas, just as the characteristics of towns, presenting as they do urban features on a small scale, bear more resemblance to those of the cities than to those of rural areas.

The rates for mental deficiency and psychopathic personality are comparatively low in the urban communities, increasing gradually with the size of the community, and are highest in the semirural

TABLE 6. *Rejection Rates for Psychiatric Disorders in Four Italian Communities of Markedly Different Population Densities.*

COMMUNITY	POPULATION DENSITY	MENTAL DEFICIENCY RATE	PSYCHOPATHIC PERSONALITY RATE	CHRONIC ALCOHOLISM RATE	PSYCHO-NEUROSIS RATE	PSYCHOSES RATE	TOTAL RATE
		%	%	%	%	%	%
C 51	60,000	5.2	6.9	1.2	4.5	.39	18.1
C 21	20,000	3.8	4.4	1.4	2.9	.60	13.1
C 89	7,000	1.0	1.8	0.8	3.9	.00	7.4
C 201	1,500	2.1	2.4	0.3	5.7	.30	10.8

With the variable factor of nationality thus controlled, the great similarity between the variations in this table and those in Tables 1 to 5 indicates how significant density is in determining both the extent and character of mental disorders, and how imperative it is, in studies of nationality, to make correction for both socioeconomic level and population density.

SIZE OF COMMUNITIES

In order to present a study of the relation of mental disorders to population density that would conform to other studies based on the size of the community rather than on its density, communities

and very dense communities. The rate for alcoholism increases in proportion to the size of the city, being lowest in semirural communities and highest in a large city (Boston). The rates for psychoneurosis, although lower than that in semirural communities, do not vary significantly in cities of different size.

Large city. In a large city (Boston), there is an extreme density not to be found in the merely urban environment. The rate for mental deficiency is increased consistently with its increase throughout the small cities. The rates for psychopathic personality and chronic alcoholism increase so sharply that the single factor of density seems inadequate

TABLE 7. *Rejection Rates for Psychiatric Disorders in Communities of Different Size.*

SIZE	SOCIOECONOMIC LEVEL	MENTAL DEFICIENCY RATE	PSYCHOPATHIC PERSONALITY RATE	CHRONIC ALCOHOLISM RATE	PSYCHO-NEUROSIS RATE	PSYCHOSES RATE	TOTAL RATE
		%	%	%	%	%	%
Semirural communities	D+	2.4	3.7	.6	4.4	.45	11.6
Towns	B	1.3	2.4	.9	3.3	.09	8.0
Small cities	C	1.5	3.0	.9	3.7	.33	9.4
Moderate-sized cities ...	C-	1.6	3.2	1.2	3.4	.35	9.8
Large city	D-	1.8	4.8	1.8	3.7	.31	12.4

were arranged on the basis of their sizes (Table 7). This not only furnished a comparable study but also served as a summary of the findings.

Semirural communities. The rates for mental deficiency and psychoneurosis are higher in these areas than in urban communities of all sizes. The rate for psychopathic personality in semirural communities is higher than that in either the small or

to account for the increase. The rate for psychoneurosis is unchanged.

COMMENT

In communities of varying size different patterns of mental diseases are present that are most significant at the two extremes, the largest city and the semirural areas.

The history of onset is practically always an infection superimposed on injured or broken skin — often the result of a slight bruise, abrasion or insect bite. The ulceration appears to be unable to gain a foothold on healthy tissue. These infections are most frequent when the troops are in combat or go out on patrol duty. Although at such times the men are usually fully clothed, they suffer scratches through their clothing. Lowered body resistance and a diet inadequate in vitamins have been suggested as factors in the etiology, but it has not been possible to confirm this theory.

PATHOLOGY

It was impossible to prepare sections for pathological examination. According to Stitt,¹ the histologic characteristics are as follows: the tissue undergoes coagulation necrosis; there is an upper layer of coarsely meshed fibrin containing degenerating polymorphonuclear leukocytes, spirochetes and fusiform bacilli; the epithelium surrounding the ulcer is thickened; its walls and base consist of granulation tissue with a surrounding area of lymphoid and plasma cells and fibrous tissue; lastly, spirochetes are found in the surrounding tissue over an area of 1 or 2 cm. — which may account for the poor results obtained by the use of local applications.

SYMPTOMS

The lesion described above soon develops a dirty-greenish-gray pseudomembrane, which is usually adherent and, on removal, reveals a relatively deep, excavated ulcer. This ulcer may become larger or remain the same size, with the formation and reformation of the membrane. The lesions are usually on the extremities, most frequently on the lower legs. They may be single or multiple, with as many as ten to fifteen on one leg. They vary from 1 to 7 cm. in diameter. The severity ranges from mild to marked, the majority of our cases being moderate. The duration in the acute cases is two or three weeks, and in chronic cases, two to three months — in some cases as long as six to eight months. Approximately 8 per cent of the cases show moderate to marked secondary infection. The ulcers are somewhat sore but not painful. Fever is absent or slight, and no constitutional reactions occur. There is no increase in the white-cell count, and the red-cell count is normal. Kahn tests of the blood serum give a negative reaction.

PROGNOSIS

These ulcers have not been watched long enough for one to observe whether they are self-limited. They probably are not, for the duration in many cases has been months, and even these cases had some treatment. The lesions heal with brown to red scar tissue. Over periods of six to eight months,

similar lesions have not faded appreciably and leave disfigurement, since the ulcer invariably extends into the subcutaneous tissue. Although its old site appears as a weak resisting point for reinfection or ultimate breakdown, this does not seem to be the case, and there have been only 2 cases in which a second lesion was superimposed on an old site.

TREATMENT

The treatment of these ulcers presented a problem. From the start it was apparent that they would not respond adequately to ordinary aseptic care. To

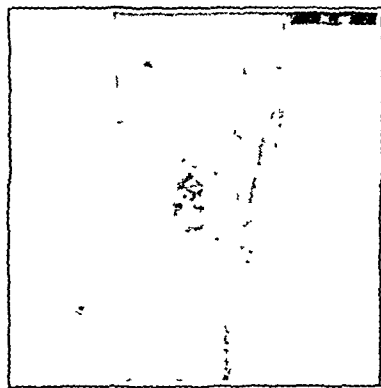


FIGURE 2. Confluence of Two Lesions.
The ulceration measured 3 by 2 cm. Note the irregular margin and the brawny induration about it.

evaluate all the forms of treatment recommended by Stitt¹ and to ascertain which was the most suitable, various medicants and procedures were used in the first half of the cases of this series. The later cases were treated by the method of choice. The more favored methods were used in a large number of test cases, and the less favored in a smaller series. At least a two-week trial was given any treatment before it was given up as having little value. The methods of treatment used were as follows.

Potassium permanganate diluted to 1:5000 and given in the form of hot packs, caused little improvement, nor did a 6 per cent solution painted on the lesions give better results.

Sodium iodide orally and *hydrogen peroxide* locally, as has been recently recommended, were tried, with no favorable results. The procedure was to give 1 gm. of sodium iodide orally three times a day. One to two hours later, when the concentration of the iodide in the blood stream was supposedly greatest, a pack of a 1 to 3 per cent solution of hydrogen peroxide, which had been made acid with acetic acid, was placed on the ulcer. Theoretically, the iodide combines with the hydrogen peroxide, setting free nascent iodine in the tissue, which acts as a bactericide.

Copper sulfate in a 10 per cent aqueous solution or a 30 per cent glycerin solution, applied locally, was ineffective.

TROPICAL ULCER

CAPTAIN MAXWELL H. FEINMAN, M.C., A.U.S.

SAN FRANCISCO

ETIOLOGY

SINCE going into operation in a South Pacific area, the dermatological service has been confronted with a type of skin ulcer that is entirely new to most of the medical officers. With little definite knowledge, and a paucity of written material on this type of skin lesion, the complete armamentarium of medical resourcefulness in this area, or as near complete as possible, has been devoted to the treatment of these patients, the main standby being the sulfonamide drugs. The ulcers eventually heal, but only after long periods of time, many lost or inefficient fighting days and a heavy attendance at sick call.

It must be remembered that for the work here reported laboratory facilities were meager, bacteriologic studies practically nil and pathological examination a scarcely hoped-for dream. Nevertheless, many tropical ulcers have been treated, all available and recommended therapeutic agents, and several that were not recommended have been tried, and definite conclusions have been reached. These are presented, together with a suggested course of treatment, for the benefit of all concerned. It is believed that such a presentation will be a definite advantage to others who have been thrown into a new environment with its own peculiarities.

The only source of detailed information on this subject to be found in the literature is Stitt's¹ *Diagnosis, Prevention and Treatment of Tropical Diseases*. I am greatly indebted to this fine book, from which I shall frequently quote.

This disease is variously known as *ulcus tropicus*, tropical sloughing phagedena and Naga sore. It consists of an acute or chronic skin lesion, of uncertain etiology but closely related to the presence of spirochetes and fusiform bacilli, and characterized by an irregular or rounded appearance, — usually the latter, — indurated edges, an excavated base, a dirty-greenish-gray sloughing membrane and red granulation tissue in the base and walls. The lesion seems to be different from that recently described by Dostrovsky and Sagher² as phagedenic ulcer, which has an undermined edge and no evidence of spirochetes or fusiform bacilli, and is best treated by the local application of sulfapyridine.

According to Stitt¹ this disease is most frequent in Amazonia, and is prevalent in India, Indo-China, southern China and the Philippines. It is said to be the chief cause of disability among laborers in Malaya, and was studied extensively by James³ in the Solomon Islands. The number of cases that find their way into the hospital is in all probability not greater than 50 per cent of the total.

The exact etiologic agent is as yet uncertain, but James³ found spirochetes in 65 to 75 per cent of the ulcers and fusiform bacilli in all. Our findings closely follow these figures. Of an appreciable number of early cases, 70 to 75 per cent showed positive smears for spirochetes. Of the later cases, only 50 per cent were positive for these organisms. Practically all the ulcers contained fusiform bacilli. Another frequent finding, which occurred in 60 per cent of the cases, was the presence of diplococci and diplobacilli that stained blue with Giemsa's stain or Loeffler's methylene blue. Gram's stain was not available, so that it could not be determined whether these organisms were gram-positive or gram-negative. In many cases, diplococci and diplobacilli were the only organisms reported.

The spirochete is a slender, delicate spirillum with a variable number of shallow undulations. It resembles and is possibly identical with *Spirochaeta vincenti*. The fusiform bacilli are plump and 5 to 7 microns in length, with straight or slightly tapered ends; they also stain blue with Giemsa's stain or methylene blue and resemble or are the same as those found in Vincent's angina. Many investigators believe that the spirochetes and bacilli are different

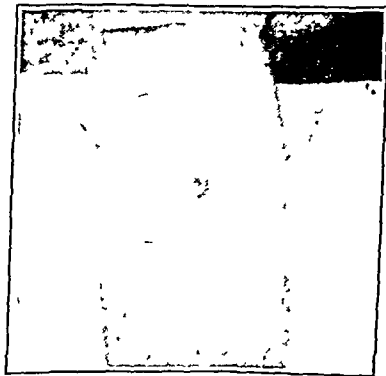


FIGURE 1. Lesion of Three Weeks' Duration (1.2 cm in diameter)
Note the indurated, raised edges

stages of the same organism. Tunnickliff⁴ states that in cultures of fusiform bacilli spirochetes appeared after five days. Smith⁵ states that he, too, has seen spiral forms take the place of fusiform bacilli in pure culture. The present findings show no evidence that a fungus is the etiologic agent.

The history of onset is practically always an infection superimposed on injured or broken skin — often the result of a slight bruise, abrasion or insect bite. The ulceration appears to be unable to gain a foothold on healthy tissue. These infections are most frequent when the troops are in combat or go out on patrol duty. Although at such times the men are usually fully clothed, they suffer scratches through their clothing. Lowered body resistance and a diet inadequate in vitamins have been suggested as factors in the etiology, but it has not been possible to confirm this theory.

PATHOLOGY

It was impossible to prepare sections for pathological examination. According to Stitt,¹ the histologic characteristics are as follows: the tissue undergoes coagulation necrosis; there is an upper layer of coarsely meshed fibrin containing degenerating polymorphonuclear leukocytes, spirochetes and fusiform bacilli; the epithelium surrounding the ulcer is thickened; its walls and base consist of granulation tissue with a surrounding area of lymphoid and plasma cells and fibrous tissue; lastly, spirochetes are found in the surrounding tissue over an area of 1 or 2 cm. — which may account for the poor results obtained by the use of local applications.

SYMPTOMS

The lesion described above soon develops a dirty-greenish-gray pseudomembrane, which is usually adherent and, on removal, reveals a relatively deep, excavated ulcer. This ulcer may become larger or remain the same size, with the formation and reformation of the membrane. The lesions are usually on the extremities, most frequently on the lower legs. They may be single or multiple, with as many as ten to fifteen on one leg. They vary from 1 to 7 cm. in diameter. The severity ranges from mild to marked, the majority of our cases being moderate. The duration in the acute cases is two or three weeks, and in chronic cases, two to three months — in some cases as long as six to eight months. Approximately 8 per cent of the cases show moderate to marked secondary infection. The ulcers are somewhat sore but not painful. Fever is absent or slight, and no constitutional reactions occur. There is no increase in the white-cell count, and the red-cell count is normal. Kahn tests of the blood serum give a negative reaction.

PROGNOSIS

These ulcers have not been watched long enough for one to observe whether they are self-limited. They probably are not, for the duration in many cases has been months, and even these cases had some treatment. The lesions heal with brown to red scar tissue. Over periods of six to eight months,

similar lesions have not faded appreciably and leave disfigurement, since the ulcer invariably extends into the subcutaneous tissue. Although its old site appears as a weak resisting point for reinfection or ultimate breakdown, this does not seem to be the case, and there have been only 2 cases in which a second lesion was superimposed on an old site.

TREATMENT

The treatment of these ulcers presented a problem. From the start it was apparent that they would not respond adequately to ordinary aseptic care. To

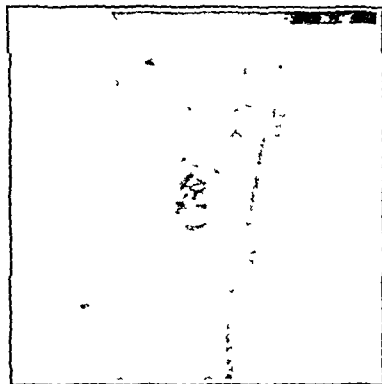


FIGURE 2. Confluence of Two Lesions.
The ulceration measured 3 by 2 cm. Note the irregular margin and the brawny induration about it.

evaluate all the forms of treatment recommended by Stitt¹ and to ascertain which was the most suitable, various medicants and procedures were used in the first half of the cases of this series. The later cases were treated by the method of choice. The more favored methods were used in a large number of test cases, and the less favored in a smaller series. At least a two-week trial was given any treatment before it was given up as having little value. The methods of treatment used were as follows.

Potassium permanganate diluted to 1:5000 and given in the form of hot packs, caused little improvement, nor did a 6 per cent solution painted on the lesions give better results.

Sodium iodide orally and *hydrogen peroxide* locally, as has been recently recommended, were tried, with no favorable results. The procedure was to give 1 gm. of sodium iodide orally three times a day. One to two hours later, when the concentration of the iodide in the blood stream was supposedly greatest, a pack of a 1 to 3 per cent solution of hydrogen peroxide, which had been made acid with acetic acid, was placed on the ulcer. Theoretically, the iodide combines with the hydrogen peroxide, setting free nascent iodine in the tissue, which acts as a bactericide.

Copper sulfate in a 10 per cent aqueous solution or a 30 per cent glycerin solution, applied locally, was ineffective.

Formaldehyde in a 7 per cent solution, applied locally, appeared to clean up the ulcer, but the latter showed no evidence of closing over.

Cleansing with *alcohol* and covering the area with an occlusive vaseline dressing, which was left in place for a period of three days, was unsatisfactory.

Human plasma in the dried form or as a four-times concentrated solution, applied locally, seemed to have some value but was eventually given up as inadequate. The dried plasma gave better results than did the solution.

Bismuth subsalicylate in daily local applications gave no favorable results. Intramuscular injections of 0.5 cc. at the start, followed by 1.0 cc. every other day for three doses and then twice a week to a limit of ten injections, showed good results if sulfanilamide powder was used locally at the same time and an occlusive vaseline dressing was applied when the ulcer appeared to be clean. The vaseline dressing was left in place for three days. Although this method often gave excellent results, it did not seem to meet the situation. The ulcers progressed to a nearly healed stage, but from then on many took a long time to heal.

Sulfanilamide or *sulfadiazine* powder used locally seemed to clean the ulcer, but there was no evidence of healing.

Neoarsphenamine, either in a 3 per cent glycerin solution or in powder form, applied locally, had little apparent effect in healing the ulcer.

Ferrous sulfate and *vitamins*. On the basis of a vitamin deficiency and lowered body resistance, the first half of the patients were given 2 gm. of ferrous sulfate daily and tablets providing 15,000 units of vitamin A, 1200 units of vitamin D, 225 mg. of vitamin C (ascorbic acid), 6 mg. of thiamine chloride, 9 mg. of riboflavine and 60 mg. of nicotinamide,

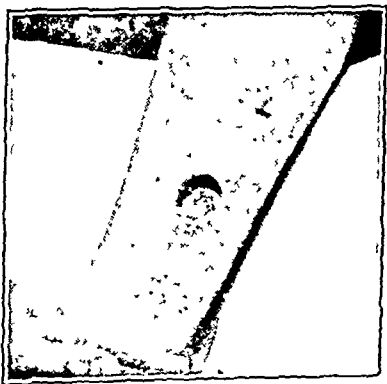


FIGURE 3. Lesion of Six Weeks' Duration (3 by 2 cm.). Note the thickened edges, the granulating base and the excavation.

to which was added 150 mg. of niacin (nicotinic acid), daily. There was no apparent improvement compared with the later cases, in which ferrous sulfate and vitamins were given only when indicated.

Periods of exposure to *sunshine* (ultraviolet rays) seemed to have no special value.

Mild *mercurous chloride ointment* was used locally. This seemed to clean the ulcer, but there was no evidence of healing.

Acridflavine in 1:1000 solution, which has been used by other investigators, and *vaccine therapy*, which has been recommended in spite of relatively unsatisfactory results, were not available. *Penicillin* was not available in quantities to warrant its use.

Mapharsen was substituted for the recommended intravenous neoarsphenamine or novoarsenobenzol. In a 0.3 per cent solution or in powdered form applied locally, it caused moderate improvement but did not close the ulcer. The best results were obtained from intravenous injections. The often seen brawny induration and soreness about the site of the ulcer disappeared after one or two injections, but the greenish-gray membrane continued to form. For this reason sulfanilamide or sulfadiazine powder was also used locally. This form of treatment gave by far the best results. In five to seven days the ulcer became clean, and the induration and soreness rapidly disappeared. In about ten days the ulcer began to appear smaller, with new epithelium growing in from the edges. At the present time, the average ulcer heals and the patient is discharged from the hospital in two or three weeks. Needless to say, aseptic dressings and technic are used. Large ulcers take longer to heal, and early or small ones respond faster than do chronic ones. The dosage used was 0.03 gm. for the first dose and 0.06 gm. for the subsequent doses. The first three doses were given three days apart and the remaining doses five days apart, for as long as indicated. Reactions to the Mapharsen occurred in only 3 cases, and were mild.

Curettage and skin grafting was not necessary in most cases. Two recent cases were curetted, solely for the purpose of removing thick, firm and heavy necrotic tissue. One of these ulcers is filling in rapidly from the bottom, and both are showing healthy granulated tissue. It is possible that these cases will do better with later skin grafting, although in a recent elderly patient a similar ulcer on the lateral aspect of the knee, 6 cm. in diameter but not deep, healed completely and firmly in six weeks, with a scar only 2.5 cm. in diameter.

Ambulatory Treatment

Recently, members of a line battalion have been treated as ambulatory patients with the method of choice, namely, intravenous Mapharsen, local sulfanilamide powder and occlusive dressings. The first patient had numerous lesions on both lower legs of superficial or moderate degree. The duration of the disease was two months, with numerous visits on sick call and little or no evidence of healing. Under treatment, with daily dressings for one week and

When every fifth day, the lesions healed in three weeks. The second case was an indurated lesion on the lower leg of three weeks' duration. This healed completely in three weeks. The third patient had several superficial ulcers on both arms of four



FIGURE 4. Lesion of Four Weeks' Duration (3.8 by 5.0 cm.). This eventually healed, with a flat scar one third size of that shown.

weeks' duration. These dried and healed following one injection of Mapharsen.

CONCLUSIONS

Spirochetes and fusiform bacilli appear to be a definite factor in the production of tropical ulcers.

These ulcers usually occur on broken or injured skin. Therefore, all troops should be cautioned about this, so that they may promptly apply a bactericide and first-aid dressing, in an effort to prevent ulcer formation at these points.

Medical officers should learn to recognize these ulcers early. They should not experiment with the easily available sulfonamide drugs or ointments, gentian violet, or Frazier's solution to see what will happen, but should proceed directly to treat vigorously with intravenous Mapharsen, and apply sulfanilamide or sulfadiazine powder to the ulcers, as their appearance or bacteriology may direct. After the ulcer has become clean, an occlusive vaseline dressing should be applied and changed infrequently.

Mapharsen can and should be made easily available to forward echelons, and treatment should be instituted in the early stages of the ulcer. In this way patients can remain ambulatory, with no loss of man-days of work or fighting and no hospitalization.

I am indebted to T/3 Basil L. Miner and T/5 Edward Puskarz, ward supervisor and wardmaster, respectively, for their interest and co-operation in the treatment and care of these patients and to T/5 Jack C. Renner for his work in smear and slide diagnosis.

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THE USE OF BLOOD IN THE TREATMENT OF DUODENAL FISTULA

PETER A. CONSALES, M.D.,* AND WILLIAM T. O'CONNELL, M.D.†

BOSTON

CASE REPORT

EXTERNAL duodenal fistula constitutes a problem of great importance: and if not corrected usually terminates fatally.¹ Fortunately, it is a rare complication. Up to 1923 only 61 cases had been reported.² In a more recent communication by Bartlett and Lowell,³ however, 128 authentic cases were presented in what was believed to be a complete review of the literature from 1865 to 1937. It is apparent that within the last two decades the prevalence of this disease has increased, perhaps owing to the greater number of operative procedures carried out in the right upper quadrant of the abdomen.

The mortality is still extremely high. Most authors consistently report an approximate mortality of 50 per cent irrespective of the procedures used, whether medical or surgical.⁴ Management along conservative measures, however, has considerably reduced the mortality.⁵ According to Kittelson,⁶ 65 cases treated conservatively had a mortality of 23 per cent. Unquestionably the latter treatment has become the procedure of choice within the last ten years, and surgery has been reserved for cases in which there is a definite indication for it.

External duodenal fistula is usually caused by injury to the duodenum during the performance of a surgical operation in the right upper quadrant of the abdomen, such as that on the duodenum itself, the pyloric end of the stomach, the gall bladder, the liver, the hepatic flexure of the colon and the right kidney.⁷ It is not intended to review the etiology in greater detail or to describe the pathologic physiology, the symptoms and the matter of diagnosis of duodenal fistula, inasmuch as these have been adequately dealt with in a recent contribution.³

In this paper is presented a case of external duodenal fistula following an operation for gall-bladder disease in which all known therapeutic methods were tried, with extremely poor results. The effects of dehydration, acidosis and the inevitable extensive and severe excoriation of the skin were so pronounced that a supposedly new method of remedying this trying situation was tried — the use of whole blood in the wound, packing the latter firmly with cotton. Following this procedure the duodenal fistula promptly ceased draining. There was immediate relief in the systemic symptoms, as well as beneficial effect on the surrounding skin, with prompt healing of the fistula.

A. S. (C 55429), a 57-year-old, married woman, was admitted to St. Elizabeth's Hospital on August 8, 1943, with a history of upper abdominal pain and vomiting of 48 hours' duration. The pain was constant, with intermittent exacerbations that had become increasingly severe. For the last few years, the patient had been in good health with the exception of vague digestive disorders, characterized by belching of gas, a bloated feeling and moderate hyperacidity. No similar acute episode had been experienced prior to this one.

On physical examination the patient was obese, weighing 179 pounds, and appeared quite ill, dehydrated and in acute pain, with marked nausea and occasional vomiting. The abdomen was distended and slightly tympanitic. On auscultation no borborygmi were noted. There was marked tenderness, with rebound pains throughout the upper abdomen, and moderate rigidity. No palpable masses were noted. The liver was not palpable. The temperature was 99.8°F., the respirations 25 and the blood pressure 128/80. The red-cell count was 4,610,000 and the white-cell count 10,000, with 76 per cent polymorphonuclear leukocytes. The hemoglobin was 90. The urine was essentially normal save for a slight possible trace of albumin.

Intravenous replacement of fluids was started, and an initial plain film of the abdomen was taken. This showed considerable gas, especially in the upper right quadrant, with mottling over the gall-bladder region that resembled calculi. The patient's general condition did not improve, and the next day a laparotomy was performed through an incision in the upper part of the right rectus muscle. Exploration revealed a small quantity of free bile in the peritoneal cavity. The greater omentum was curled around and adherent to the first and second portions of the duodenum. It was freed by sharp dissection, revealing the first and second portions of the duodenum, which were firmly adherent to the inferior surface of the liver. To expose the gall bladder and its ducts, the adherent duodenum was in turn freed from the liver.

Despite the utmost care in exposing the deeper tissues, which were quite friable, a rent of 2 cm. occurred in the duodenum. This was quickly closed. Two rows of intestinal sutures and a third of linen were used, and the opening was securely covered with omentum. The gall bladder was contracted, cordlike and almost fused into the liver bed; eight stones were extracted. The common duct was of normal size and no stones were palpable. The cystic duct was doubly ligated and divided with a cautery. The contracted, sclerotic gall bladder was so firmly incorporated in the liver tissue that removal was not attempted because of the extent of liver damage inherent in such procedures. Five grams of sulfanilamide was sprinkled in the abdomen. A Penrose drain was inserted in Morrison's pouch and brought out through the lower end of the incision, and the abdomen was closed. The immediate postoperative convalescence was complicated by a bronchopneumonia that cleared up 7 days later with the aid of sulfonamide therapy.

On the 3rd postoperative day, the Penrose drain was withdrawn and only a small amount of bile drainage was noted. On the following day, a greater amount of bile-stained drainage was present and soon increased. The character of the drainage had changed and a marked excoriation of a large abdominal area about the incision had occurred, establishing the diagnosis of duodenal fistula. On the 5th postoperative day, the drainage was profuse and the upper part of the wound had sufficiently separated to permit a clear view of two fistulous openings, the larger one measuring 6 by 2 mm. and the smaller 3 by 2 mm. The skin was protected by equal parts of kaolin and zinc-oxide ointment. Dressings had to be changed every 1 or 2 hours, despite continuous suction

*Assistant surgeon, St. Elizabeth's Hospital.

†Formerly, intern, St. Elizabeth's Hospital.

and an indwelling nasal tube. Donald's⁸ method* was then tried for 3 days, but there was no appreciable relief and the drainage did not diminish. The patient became increasingly weak and was maintained on intravenous therapy. During drainage, particles of undigested food were present and even fruit juices were frequently observed.

Since the methods advocated for this condition had failed, an attempt was made to devise a method that would block the escape of duodenal contents. Packing was considered as holding the possibility of success provided something was used about the packing to prevent leakage. A report on the treatment of leg ulcers with whole blood⁹ gave sufficient impetus to try whole blood and packing empirically. Twenty days postoperatively (15 days after the diagnosis of duodenal fistula had been established), this method was initiated.

The method devised is simple. From 3 to 5 cc. of the patient's blood is procured from an arm vein in a sterile syringe. The abdominal wound is wiped thoroughly dry with gauze, and 2 cc. of blood is sprayed into the bottom of the wound. A wad of cotton is firmly packed against the sinus or sinuses at the bottom of the wound. A little more blood is sprayed around the periphery of the cotton packing. Several layers of cotton may be used, and each time blood is sprayed at the periphery; enough cotton is employed to fill the wound flush with the skin. Two straps of adhesive plaster are applied not too firmly. In this case the wound was so excoriated that no adhesive was used for several days. The outer dressing is changed daily, but the packing is removed every 2 or 3 days.

Following the institution of this method, a marked change was evidenced. During the next 48 hours only serous dampness was noted on the abdominal dressing. The patient's general condition improved, and her appetite and strength likewise increased. On removing the packing it was found to be firmly adherent to the walls of the wound, and healthy granulations were evident. A biopsy specimen from the wall of the fistula was submitted for pathological examination, which was reported as follows:

One corner of the specimen shows stratified squamous-cell epithelium. Underlying and at the margin there is a layer of granulation tissue densely infiltrated with lymphoid cells, polymorphonuclear leukocytes and a few eosinophils. The tissue is moderately vascular. Diagnosis: granulation tissue (Fig. 1).

From then on the wound was repacked every 48 hours. The patient improved steadily and the skin slowly healed. She was out of bed and walking about on September 6, and was discharged on September 12, 34 days postoperatively. At the time of discharge the hitherto gaping abdominal wound was about half its original size and a firm packing was left in situ. From then on convalescence was uninterrupted, with complete healing of the fistula 3 weeks later.

DISCUSSION

Closure of the duodenal defect in duodenal fistula may be accomplished either by operative or by nonoperative measures.¹⁰ Operative procedures have not been encouraging in that surgical intervention is usually carried out at a time when the patient's condition is extremely poor. For such reasons most writers agree that surgery should be reserved for selected cases.¹¹ Furthermore, most

authors are in accord that at present the best hope in dealing with this aggravating complication lies in palliative and conservative measures.¹² A number of methods have thus far been advocated, each



FIGURE 1. Photomicrograph of the Biopsy Specimen. Note the granulation tissue.

with reported successes. The basic principles underlying those generally carried out can be concisely summarized as follows:

Mechanical:

Elimination of positive duodenal pressure by the passage of a tube into the duodenum. This is impossible in the case of a leak from a duodenal stump after gastric resection.

Absorption of the ferments, achieved by the production of an acid medium by continuous irrigation of the wound with a tenth-normal solution of hydrochloric acid, with citric acid, or with 5 per cent solution of tannic acid.

Absorption of the ferments by the application of finely divided charcoal, kaolin or bronzing powder.

Removal of the fluids by continuous suction obtained by a tube inserted in the fistula. (In a modification of this method two tubes are used — one for irrigation of the fistula with peptone water, beef juice and the like, and the other for suction.)

Chemical:

Neutralization of the proteolytic ferments by combining them with an excess of peptone powder, protein, beef juice or similar agents, also whole milk thickened by adding acidophilus bacillus.

Protective:

Protection of the surrounding skin by the application of kaolin and glycerin ointment, boric ointment, liquid latex or the like.

In every method an attempt is made to remove the intestinal digestive contents that constantly

*Donald, not being satisfied with the methods at hand, has described a simple apparatus that he used successfully in a patient who developed a fistula from the duodenal stump twelve days after a subtotal resection of the stomach and a posterior Polya type of anastomosis. The fistula was completely obliterated eight days after the apparatus was applied. Donald's method, in brief, is as follows: A cuff is made from a round standard apertum container, the bottom of which is cut off, the container being firmly applied about the wound and strapped to the skin. A thick ointment composed of 50 per cent glycerin and 50 per cent kaolin is then heavily applied to the inside wall of the container and to the skin adjacent to the fistula. The fluid that drains into the box is aspirated once every hour and subsequently at gradually lengthening intervals, as required. When aspiration is not being carried out, the box is closed tightly by insertion of the lid of the container. The patient is then free to move about in bed as he desires.

pour out of the wound, and whenever possible to collect these juices and feed them back to the patient through an indwelling nasal tube or a jejunostomy. The use of solutions to neutralize chemically the intestinal discharges is in many cases of little value. The application of protective ointments is also of limited value, depending on the character and amount of drainage. Those who have had experience with the persistent drainage from duodenal fistulas realize the many disadvantages inherent in the above methods. Unquestionably the desirable objective is to keep the wound absolutely dry and free from digestive juices if possible, with the hope of aiding the formation of granulation tissues, thus finally obliterating the fistula.

In the present case, this objective was attained by using autogenous blood around the periphery of cotton packing within the fistulous wound. It is realized that the report of a single case is insufficient to warrant any conclusions; yet it seems certain that in this case the rapid growth of granulations obliterating the duodenal defect can be attributed to the use of whole blood.

This appears to be in conformity with the observations of Moorehead and Unger¹³ on the use of residual red cells from different blood groups. They have mixed these and stored them in a refrigerator from a few days to a few weeks, obtaining a gelatinous mass. This they have used as a dressing material for wounds such as open joints, infections, burns and ulcers. The material is reported to aid the ingrowth of new tissues when applied to certain wounds. Seldon¹⁴ has likewise used this gelatinous mass of red cells in postoperative wounds, with encouraging results. In addition, to

eliminate the disadvantage of absorption by the gauze, he has evolved a method of reducing the semiliquid mass of red cells to a fine powder, which is dusted on the wound or applied by a spatula. Seldon's report is encouraging in that the postoperative period is materially reduced.

SUMMARY

Duodenal fistula and its treatment is briefly discussed, and a case is presented.

The treatment of this case by whole blood, topically applied, is described, and the result obtained is discussed.

It is hoped that this method may be applied by others in this trying and serious condition.

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MEDICAL PROGRESS

PARENTERAL-FLUID THERAPY*

I. Estimation and Provision of Daily Maintenance Requirements

ALLAN M. BUTLER, M.D.,† AND NATHAN B. TALBOT, M.D.‡

BOSTON

THE last fifty years have witnessed a steady increase in knowledge concerning the metabolic disturbances resulting from starvation and dehydration. In addition, the increased availability of a variety of parenteral solutions and specific nutrients has increased not only the possible effectiveness of parenteral nutrition and repair therapy but also the physician's responsibility in the administration of parenteral fluids. The purpose of this review is to present in outline form such basic data as may be helpful in effectively utilizing his knowledge in the provision of the parenteral therapy that is at hand today or may become available tomorrow. The first part deals with the

rate and his relatively greater load of catabolites presenting for urinary excretion. These large volumes may also be due to a somewhat limited concentrating ability of the kidneys.^{3,4} The urine volumes given in the table appear adequate to provide the volumes required to excrete the increased total osmimoles⁵ that may present for renal excretion incident to operation, traumatic shock, fever, starvation or the debility of illness.⁶⁻¹³ Patients with a renal impairment that limits concentrating ability may have an obligatory renal water loss that is 100 per cent greater than those given in the table.¹⁴ Moreover, insensible water losses as much as 100 per cent above those recorded

TABLE 1. *Approximate Normal Water Losses and Allowances* per Day for Persons of Varying Size Not Subject to Excretion or Sweating.*

SIZE	WATER LOSS				USUAL WATER ALLOWANCES		
	URINE cc.	STOOL cc.	INSENSIBLE cc.	TOTAL cc.	cc./person	cc./kg	oz./lb.
Infant (2-10 kg.)	200-500	25-40	75-100†	300-640	330-1000	165-100	2 5-1 5
Child (10-40 kg.)	500-800	40-100	300-600	840-1500	1000-1800	100-45	1 5-0 7
Adolescent or adult (60 kg.)	800-1000	100	600-1000‡	1500-2100	1800-2500	45-30	0.7-0 5

*Including the water content and water of oxidation of food, which under normal circumstances, except for infants, approximates the insensible water loss.

†1.3 cc. per kilogram per hour.²

‡0.5 cc. per kilogram per hour.²

estimation and parenteral provision of the daily maintenance requirements of patients who cannot be nourished enterally. The second part will cover the estimation of losses incident to dehydration and the provision of parenteral repair therapy.

ESTIMATION OF DAILY MAINTENANCE REQUIREMENTS

A consideration of maintenance requirements is an obvious prerequisite to logical parenteral maintenance therapy.

Table 1 presents the approximate daily water losses of normal infants, children and older persons who are not performing work or sweating. It should be noted that the infant has a greater water loss per kilogram of body weight than does the adult. His greater insensible loss^{1,2} is associated with his relatively larger surface area and higher metabolic rate; and his greater urine volume per kilogram reflects the infant's higher metabolic

rate and his relatively greater load of catabolites presenting for urinary excretion. These large volumes may also be due to a somewhat limited concentrating ability of the kidneys.^{3,4} As such abnormal losses are not unusual for patients requiring parenteral therapy, their occurrence demands appropriate extra allowances of water above those listed in Table 1. Extreme extrarenal water losses (2000 to 5000 cc.) may be suffered by patients subject to high environmental temperatures.^{1,19-22}

The data of Tables 2 and 3 approximate the normal daily allowances of sodium chloride and

TABLE 2. *Approximate Normal Sodium Chloride Maintenance Allowances Per Day for Resting Nonsweating Persons of Varying Size.*

SIZE	SODIUM CHLORIDE	
	gm.	cc.
Infants	1	125
Children	3	350
Adolescents and adults	6	700

the daily basic caloric, carbohydrate and protein requirements for persons of various sizes lying in bed and thus inactive. Worthy of special note is

*From the Children's Medical Service, Massachusetts General Hospital, and the Department of Pediatrics, Harvard Medical School.

†Chief of the Children's Medical Service, Massachusetts General Hospital, and associate professor of pediatrics, Harvard Medical School.

‡Assistant physician, Children's Medical Service, Massachusetts General Hospital, and associate in pediatrics, Harvard Medical School.

the fact that such daily sodium chloride needs of infants and adults are satisfied respectively by approximately 125 and 700 cc. of physiologic saline solution. The therapeutic implication of these small maintenance needs of saline solution has been emphasized.^{15-17,23-26} Should all the infant's or adult's parenteral fluid contain 0.85 per cent of sodium chloride, each would obtain approximately 6 or 22 gm. respectively of the salt per day. Such an excess of parenteral solution often results in fluid retention and in a urine volume that is extremely small relative to the fluid intake.^{15-17,26} This normal

in both the renal and extrarenal loss of water.^{1,11} Excessive intravenous dextrose should, however, be avoided because of the possibility of overburdening the liver³⁴ and of inducing an undue hyperglycemia, glycosuria and polyuria. Again, as mentioned in considering Table 1, the allowances of Table 2 and the requirements of Table 3 do not include the repair of losses incident to shock, trauma or illness.

The provision of the protein allowances specified in Table 3 can be accomplished by whole blood or plasma transfusions and the infusion of solutions

TABLE 3. *Approximate Daily Caloric Requirements of Normal Resting Persons of Varying Size, Together with the Daily Dextrose and Amino Acid Allowances* That Theoretically Might Satisfy Them.*

SIZE	DAILY CALORIC REQUIREMENT		DAILY DEXTROSE ALLOWANCE		DAILY AMINO ACID ALLOWANCE	
	cal./kg.		gm./kg.	cal./kg.	gm./kg.	cal./kg.
Young infants	60		14	54	1.5	6
Old infants	55		13	51	1.0	4
Children	30		7	28	0.6	2
Adolescents and adults	25		6	24	0.6	2

*Available evidence suggests 6 gm. of nitrogen or 40 gm. of amino acid as a reasonable daily allowance for the adult; that for estimating the daily allowances for young resting patients on a high carbohydrate diet is meager.

response is not infrequently falsely interpreted as an indication for more fluid or of circulatory failure or renal insufficiency. In patients receiving a sulfonamide, such an oliguric response to excessive saline solution may be attributed to a deleterious effect of the drug on the kidneys and may result in the discontinuance of a highly desirable therapy. If, on the other hand, the drug is continued, the low urine volume may actually result in an avoidable sulfonamide hematuria—avoidable because the infusion of the same volume of proper parenteral fluids would have provided a urine volume sufficient to allay such a complication.

Whereas the provision of water and sodium chloride allowances is readily accomplished parenterally, the parenteral administration of the normal caloric and protein allowances present more difficulty.

Because in the past dextrose has been more readily available than amino acids, protein or fat for parenterally satisfying caloric requirements, it has usually been used as the source of the major portion of the calories supplied by this route. In so far as parenteral dextrose has satisfied the caloric needs, it has reduced body tissue and nitrogen loss and accomplished a body-protein sparing effect. Today, however, at least the basic protein needs can be readily met by such amounts of parenterally administered amino acids as specified in Table 3.^{8,27-33} The allowances of dextrose given in the table are those required to approximate the basic caloric requirements and thus theoretically effect minimal nitrogen or amino acid requirements. The reduction of protein metabolism to such minimal levels should limit the specific dynamic action of protein and the metabolic rate and provide an economy

of amino acids. In the presence of a significant anemia, whole-blood transfusions are specifically indicated. Plasma transfusions should be employed in the presence of a reduced plasma volume and increased red-cell count, hematocrit or hemoglobin concentration. Although mixtures of the pure amino acids that provide the ten essential to man, together with glycine, have been shown to be effective in maintaining nitrogen balance^{35,36} and to be nontoxic even when injected rapidly,^{36,37} such mixtures are not as yet available for general use. A commercially available enzymatic hydrolysate of casein and pancreatic tissue providing approximately 80 per cent of the total nitrogen as amino acids and 20 per cent as dipeptide* has been shown to be effective in the parenteral provision of basic nitrogen allowance^{8,27-31,33} and superior to such acid hydrolysates as are available for general use today.³⁷⁻³⁹ The enzymatic hydrolysate, however, has definite limitations. If it is infused at more than a moderate rate, nausea, vomiting, hyperpyrexia, polyuria and thrombosis of the vein and edema of the extremity receiving the infusion may occur.^{8,28-31,33,40} Such reactions and the fact that urinary nitrogen may be double that which pertains with the infusion of equivalent amounts of plasma⁴¹ suggest that this preparation might be improved. For the present, reasonable prerequisites to the parenteral administration of amino acids appear to be as follows.

The patient must be unable to ingest sufficient food enterally to meet his caloric and protein requirements.

*The amino acid product known as Amigen (Mead, Johnson and Company).

His basic caloric requirements as specified in Table 3, must be covered sufficiently by par-enteral dextrose,³⁷ with or without fat, properly emulsified for intravenous administration⁴²⁻⁴⁶ to accomplish effective sparing of endogenous nitrogen.

The amino acids should be added to the par-enteral dextrose solutions so that their concentration in the infusion does not appreciably exceed 3.5 per cent and so that the reaction of the solution is approximately pH 6.5.^{8,33} The volume and dextrose content of the infusion will then prescribe a rate that will limit such reactions as listed above.

The total amount of amino acid thus administered should depend on the estimated nitrogen loss sustained by the patient, whose endogenous nitrogen metabolism is being kept minimal by the intravenous infusion of such dextrose and possibly fat as can be effectively utilized. Under such conditions the average daily nitrogen loss in the adult may approximate 6 gm. but may vary from 4 to 20 gm.^{6-11,39} Therefore, approximately 40 gm. of amino acids ($40 \div 6.25 = 6.4$ gm. of nitrogen) will be required per day to cover the average nitrogen loss. In exceptional circumstances double the above requirements of amino acids may be included in the dextrose infusion.

Figure 1 shows the quantities of intravenously administered physiologic saline solution, 5 per

3. It is seen that, if the caloric requirements are to be provided, all the fluid must contain 10 per cent dextrose unless the water intake is to be excessive or unless fat or more amino acids are included in the infusion.

Figure 2 depicts the amounts of such intravenous fluids that will cover the daily requirements of

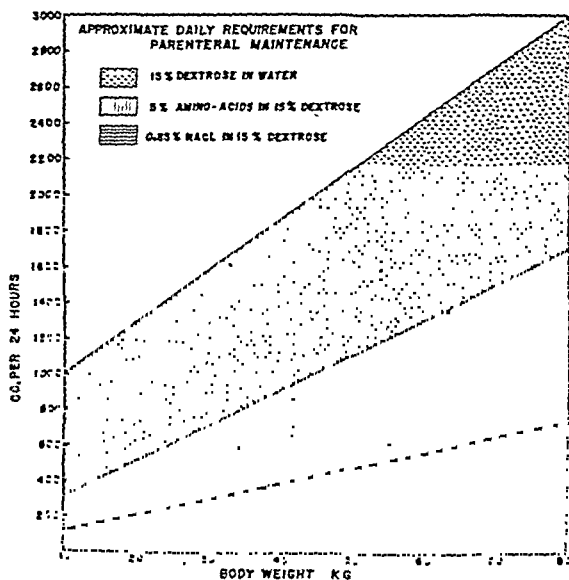


FIGURE 2.

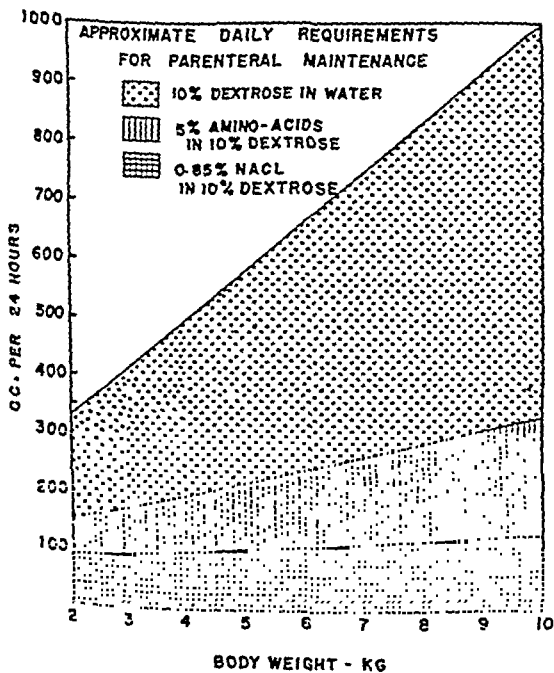


FIGURE 1.

patients who are heavier than those included in Figure 1. The dextrose concentration has been increased to 15 per cent, since provision of the dextrose allowance (Table 3) by a 10 per cent solution would require the infusion of excessive fluid unless the patient is so dehydrated as to need many cubic centimeters of extracellular fluid or unless fat or more amino acids are included in the infusion.

Because thiamine deficiency may occur within a period of two weeks^{47,48} and because the thiamine requirements may be proportional to the carbohydrate intake,⁴⁹ it seems reasonable to add from 2 to 5 mg. of thiamine per day — depending on the size of the patient — to the glucose infusions. Although there is evidence³⁹ that vitamin deficiencies other than that of thiamine do not develop within several weeks, pre-existing nutritional deficiency or infection may suggest the advisability of providing 0.5 to 0.3 mg. of riboflavin, 5 to 30 mg. of niacinamide and 30 to 100 mg. of ascorbic acid per day. Since these vitamins are unstable in alkaline solution, they should not be added to alkaline solutions.

To support and supplement such maintenance therapy, whole-blood or plasma transfusions should be given as specifically indicated by anemia or by a low concentration of serum proteins.⁵⁰⁻⁵² If par-enteral therapy is required for more than four or

cent amino acids and 10 per cent dextrose that will cover the daily water, salt, caloric and protein requirements of infants as given in Tables 1, 2 and

five days, the desirability of a transfusion of 10 cc. of whole blood or 15 cc. of plasma per kilogram of body weight should be considered. Unless the hemoglobin concentration of the blood is above normal, whole-blood transfusions appear to sustain blood and plasma volumes better than do plasma transfusions.⁵³⁻⁵⁵

Finally, even though such parenteral therapy includes amino acids and vitamins as specified above, it is nutritionally inadequate as regards many intracellular needs, so that the desirability of starting, as soon as possible, oral feedings that supply these intracellular needs should be constantly kept in mind.⁵² Fat-free beef broth and small amounts of milk diluted with an equal volume of water or with some such fluid as ginger ale provide appropriate initial oral nourishment.

MANNER AND RATE OF PARENTERAL ADMINISTRATION

If such are the types and amounts of parenteral fluids required to support the daily maintenance requirements, how should they be administered? Since only solutions given intravenously should contain more than 2.5 per cent dextrose, provision of sufficient dextrose by clysis to provide the basic calories is impracticable. The limitations of so-called "sets" of short infusions and clyses as compared to continuous-drip infusions are illustrated for the infant in Figure 3 and for the adult in Figure 4.

It is readily seen in Figure 3, column A, that a continuous infusion such as that outlined for the 5-kg. infant in Figure 1 closely approximates 100 per cent of the daily water, sodium chloride, caloric and protein requirements. On the other hand, as shown in column B, two short infusions of 20 cc. per kilogram of 10 per cent dextrose in distilled water and two clyses of 30 cc. per kilogram of 0.85 per cent saline solution provide only 85 per cent of the water and 30 per cent of the caloric requirements while overdosing the infant with 260 per cent of the sodium chloride requirement. The substitution of 2.5 per cent dextrose in 0.45 per cent sodium chloride solution as given in column C, for the saline clyses of column B reduces the excessive sodium chloride to 130 per cent of the requirement but still provides only 40 per cent of the daily caloric and 85 per cent of the daily water requirements. Thus, for infants, intravenous infusion is the route of choice in the parenteral provision of the daily requirement of those for whom enteral nutrition is contraindicated. The infusions are usually given most successfully into a scalp vein, the head being immobilized by sandbags and the arms and body by blankets or restraints.⁵⁶

In Figure 4, column E, it is seen that three clyses of 0.85 per cent saline solution, 12 cc. per kilogram, which provide an appropriate water intake, exceed the sodium chloride requirement by 320 per cent and provide no calories whatever.

If the clyses contain 2.5 per cent dextrose in per cent sodium chloride solution (column F), sodium chloride still exceeds the requirement

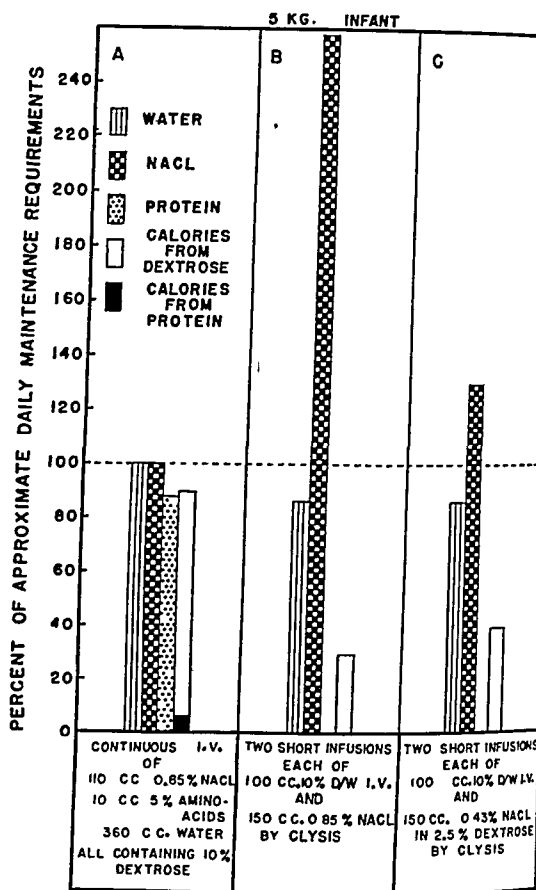


FIGURE 3.

160 per cent, whereas the calories have been increased to only 14 per cent of the daily requirement. Therefore, the provision of more calories requires the intravenous infusion of some glucose. Since a continuous drip, such as given in column A, satisfies the requirements of water, sodium chloride, calories and amino acids, resort to clyses together with small infusions in the provision of maintenance needs to adults should be avoided if possible.

What, then, is the rate at which these infusion should be administered? It has been suggested that only 10 to 12 gm. of dextrose can be oxidized per hour by an adult and that this rate prescribe a limit to the desirable rate of infusion.⁵⁷ If so only 288 gm. of dextrose should be given a 60-kilo gram adult in twenty-four hours. If this amount of dextrose is given in 2600 cc. of fluid, it means an 11 per cent solution of dextrose administered at the rate of 1.8 cc. or 32 drops a minute for twenty-four hours. Even if the rate of oxidation of dextrose by the infant is assumed to be double that of the adult, the limiting rate for a 5-kilogram

infant would be 2 gm. per hour. In twenty-four hours of continuous infusion only 48 gm. of dextrose could be provided. If this dextrose were provided in the 700 cc. of daily fluid requirement, the concentration of dextrose would be approximately 7 per cent and the rate of infusion 0.5 cc. or 9 drops per minute for twenty-four hours. Thus, for both adults and infants, only approximately 10 per cent of the basic daily calories can be provided by parenteral dextrose if such immediate oxidative capacity is the limiting factor. Infusion rates above these limits appear to be accompanied by an increased storage of glycogen and possibly by such as occurs when similar amounts of carbohydrate are ingested orally. Since most patients receiving parenteral-fluid therapy have suffered some nutritional depletion, the infusion of dextrose at rates that exceed those of its immediate oxidative utilization may be beneficial rather

than out significant hyperglycemia and glycosuria. For the 60-kilogram adult this would mean 48 gm. of dextrose (not 10 to 12 gm.) per hour. Thus, eight hours of infusion would provide 384 gm. and the basic caloric needs of approximately 1500 calories as given in Table 3. Obviously, the continuation of such a rate of dextrose infusion over longer periods of time would provide excess dextrose and calories ($48 \text{ gm.} \times 24 = 1052 \text{ gm.}$ or 4200 calories) and might result in considerable glycosuria.^{23,34, 58, 59}

Acceptance of 0.8 gm. per kilogram per hour as the upper limit of desirable rate of dextrose infusion means that the infusion of such a daily requirement as 70 gm. of dextrose in 700 cc. of fluid to a 5-kilogram infant requires a continuous drip containing 10 per cent dextrose at approximately 0.7 cc. or 13 drops per minute for seventeen hours. For the 60-kilogram adult, the infusion of a daily requirement of approximately 400 gm. of dextrose in 2600 cc. of fluid requires a drip containing approximately 15 per cent dextrose at approximately 5 cc. or 90 drops per minute for nine hours. Since the infusion of 10 to 20 cc. of 5 per cent dextrose per minute for several hours has only a slight accumulative effect on the blood volume⁶¹⁻⁶³ or plasma concentration^{15,16, 26} of the adult, the infusion rates specified above appear rather conservative^{39, 58, 59, 61} unless infection, trauma or cardiovascular function predisposes to pulmonary edema or cardiac failure.^{17, 23-26, 63} Somewhat more rapid rates of infusion over shorter periods, although causing a qualitatively impressive glycosuria, usually result in the urinary excretion of but 2 to 10 per cent of the dextrose injected.^{59, 61} In spite of the fact that such a glycosuria is generally thought to be dehydrating, its diuretic effect may be confined to a very minor increase in urine volume, sodium, chloride and other constituents above that which would usually result from the infusion in the absence of glycosuria.^{17, 26, 59} The factors affecting the not infrequently observed variation in the degree of hyperglycemia and glycosuria resulting from such rates of infusion have not been well defined. Infection, temperature and state of nutrition probably play an important role. Since glycogen has a high potassium content,⁶⁴ the amount of potassium available for combination with dextrose may be a factor in the deposition of glycogen. The amount of phosphorus or cellular enzymes may limit the oxidative utilization as well as the storage of dextrose. Trauma may affect carbohydrate metabolism as much as it does that of nitrogen.^{59, 65, 66} Even though the daily requirements may be given to the adult in nine hours with but little glycosuria, a better utilization of the water and other constituents and greater comfort of the patient might be obtained by administering half the daily requirement by an infusion from 8 a.m. to 12:30 p.m. and the remaining half by an infusion

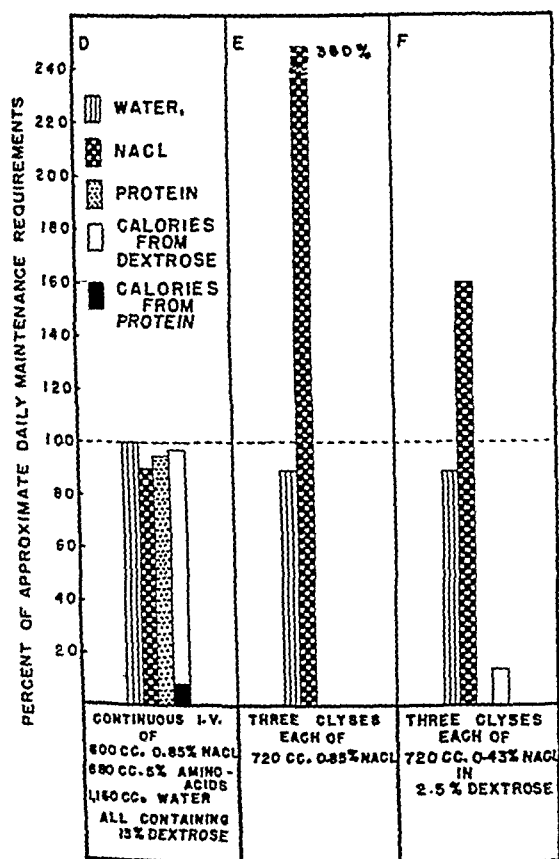


FIGURE 4.

than harmful if the infusion results in only moderate hyperglycemia and glycosuria without cardiac embarrassment or pulmonary congestion and if the daily amount of dextrose so given does not exceed the daily caloric requirement.³⁴

It has been suggested^{23, 58, 61} that dextrose may be infused for six to twelve hours at a rate of approximately 0.8 gm. per kilogram per hour with-

five days, the desirability of a transfusion of 10 cc. of whole blood or 15 cc. of plasma per kilogram of body weight should be considered. Unless the hemoglobin concentration of the blood is above normal, whole-blood transfusions appear to sustain blood and plasma volumes better than do plasma transfusions.⁵³⁻⁵⁵

Finally, even though such parenteral therapy includes amino acids and vitamins as specified above, it is nutritionally inadequate as regards many intracellular needs, so that the desirability of starting, as soon as possible, oral feedings that supply these intracellular needs should be constantly kept in mind.⁵² Fat-free beef broth and small amounts of milk diluted with an equal volume of water or with some such fluid as ginger ale provide appropriate initial oral nourishment.

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In Figure 4, column E, it is seen that three clyses of 0.85 per cent saline solution, 12 cc. per kilogram, which provide an appropriate water intake, exceed the sodium chloride requirement by 320 per cent and provide no calories whatever.

If the clyses contain 2.5 per cent dextrose in 0 per cent sodium chloride solution (column F), sodium chloride still exceeds the requirement

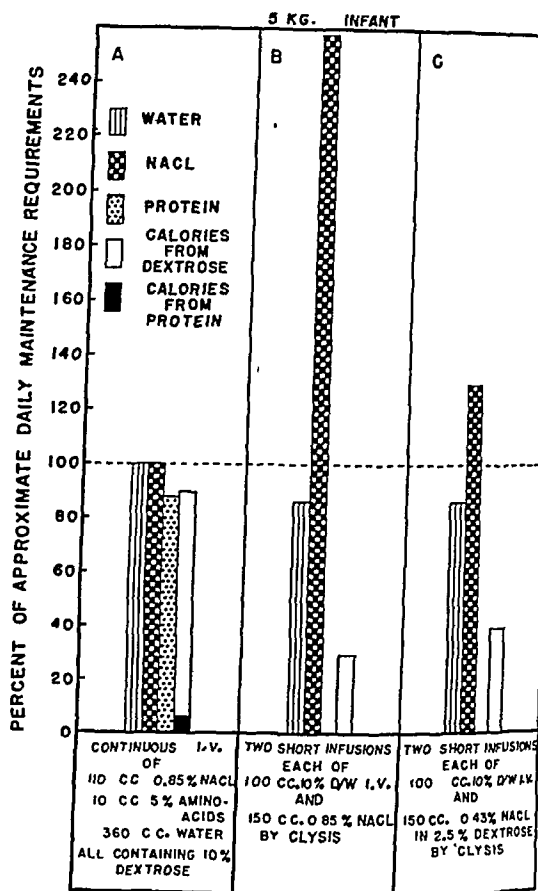


FIGURE 3.

160 per cent, whereas the calories have been increased to only 14 per cent of the daily requirement. Therefore, the provision of more calories requires the intravenous infusion of some glucose. Since a continuous drip, such as given in column D satisfies the requirements of water, sodium chloride, calories and amino acids, resort to clyses together with small infusions in the provision of maintenance needs to adults should be avoided if possible.

What, then, is the rate at which these infusions should be administered? It has been suggested that only 10 to 12 gm. of dextrose can be oxidized per hour by an adult and that this rate prescribes a limit to the desirable rate of infusion.⁵⁷ If so, only 288 gm. of dextrose should be given a 60-kilogram adult in twenty-four hours. If this amount of dextrose is given in 2600 cc. of fluid, it means an 11 per cent solution of dextrose administered at the rate of 1.8 cc. or 32 drops a minute for twenty-four hours. Even if the rate of oxidation of dextrose by the infant is assumed to be double that of the adult, the limiting rate for a 5-kilogram

NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-THIRD ANNIVERSARY

House of Delegates, May 15 and 16, 1944 (Concluded)

Report of the Committee on Medical Economics

New Hampshire Physician Service

In conjunction with the officers of the Society, the committee has continued its efforts toward the setting up of a medical-service program in New Hampshire in accordance with the instructions given to the committee at the last regular meeting of the House of Delegates. Since then progress reports have been presented at two special meetings of the House of Delegates and the approval of the House secured at each occasion. The proposals of your committee on a medical-service program have now been put into concrete form as outlined below:

Present status. The New Hampshire Physician Service has been legally incorporated under the laws of New Hampshire, our committee, with the addition of Attorney Frank J. Alloway, acting as incorporators. The incorporators have selected a group of voting members of the corporation, and these in turn have elected a Board of Directors. Since the enabling act specifies that a majority of the Board of Directors shall be approved by the New Hampshire Medical Society, it will be the duty of the House of Delegates at this session to vote on the list of directors submitted to it.

Subscriber contracts and physician contracts have been drawn up and copies of these sent to each member of the New Hampshire Medical Society. The program has been explained and discussed before each county medical society by a member of your committee, and the signed contract of the individual physicians together with subscription toward a capital fund has been solicited. Another provision of the enabling act requires the participation of at least 50 per cent of the physicians in any given area before the plan can be put into operation in that area.

Organization of the corporation. The corporation consists of three classes of persons: voting members, subscribing members and participating physicians.

Voting members consist of not less than fifteen nor more than thirty members of the New Hampshire Medical Society and not less than fifteen nor more than thirty representatives of the general public, the numbers from the two groups being equal. The original voting members are elected by the incorporators and the body is then self-perpetuating.

A subscribing member is any person who subscribes to the capital fund of the organization.

A participating physician is any physician holding a license to practice medicine in New Hampshire who is a member in good standing of the New Hampshire Medical Society, and with whom the corporation has a contract under the medical-service plan.

The Board of Directors, consisting of not less than seven nor more than seventeen members, is elected annually by the voting members of the corporation. A majority of the directors must be approved by the House of Delegates of the New Hampshire Medical Society.

The Professional Committee, consisting of not less than three members of the Board of Directors and the majority of the committee being members of the New Hampshire Medical Society, has supervision over all medical aspects of the Plan.

Subscriber contract. Contracts are written on an indemnity basis whereby the subscriber receives a specified allowance against the bill rendered by the physician. Such allowances are made in accordance with a published schedule of benefits. It is to be emphasized that this is not a fee schedule. The physician's fee is arranged between the patient and the physician as at present, subject only to the moral obligation on the part of the doctor when dealing with a patient in the low-income group to set a fee approximately equal to the benefit allowed.

The surgical contract provides for the payment of the stated benefit in the event of surgical care received in home, office or hospital. In addition, an allowance of \$10 is made

for anesthesia for any one illness, one of \$25 for diagnostic x-ray examination, and one of \$15 for laboratory examinations in any contract year, it being provided that these diagnostic examinations must be directly related to the surgical condition.

Medical indemnity is provided as a rider to the surgical contract. It furnishes an allowance of \$2 for each office and hospital visit and \$3 for each home visit in any nonsurgical condition. The first two calls in any one illness are excluded, and not more than twenty-five visits are allowed to the subscriber per year, nor more than fifteen visits to a dependent. In addition, the allowance for x-ray and laboratory examinations is made available for medical as well as surgical conditions.

Physician contract. The physicians agree to provide services to subscribers under the contract, and the corporation agrees to reimburse them in accordance with the schedule of benefits. The physician further agrees that if the money available for the payment of physicians' bills is less than the total amount of the bill, he will accept a pro rata payment of the indemnity.

Capital fund. It is estimated that a capital of \$10,000 to \$12,000 will be necessary to meet initial costs and current expenses until the volume of insurance written is sufficient to cover expenses. This fund is being raised by the solicitation of loans that shall be unsecured and noninterest bearing, and payable at the discretion of the Board of Directors when the financial condition of the corporation permits. These loans are being solicited mainly from the members of the New Hampshire Medical Society.

Comments. The plan presented has been developing over a period of three years at the instigation and with the approval of the House of Delegates of the New Hampshire Medical Society. It is interesting to note that the American Medical Association and the National Physicians' Committee are now urging the establishment of medical-service plans by component medical societies.

In regard to the specific details of the plan proposed, the indemnity type of contract was decided on because it makes no interference with the present physician-patient relation, either professional or financial.

The feasibility of providing surgical and medical care in the hospital has been demonstrated by various plans now in operation. The advisability of extending surgical care coverage to the home and office is less widely accepted.

The inclusion of medical care in the home and office is frankly experimental. It has been shown by past experience in such plans that the majority of people are interested in protection against major illnesses that may be catastrophic for them, rather than in protection against minor, relatively inexpensive illnesses. Nevertheless, if the need for the provision of medical service for the low-income groups is to be fully met, complete medical coverage must eventually be provided. The medical coverage provided in the contract is an attempt to work toward this ideal. It is restricted in amount and it is sold only as a rider to the surgical contract in order to protect the financial stability of the corporation. It is hoped, however, that through this limited coverage experience will be accumulated on which to base further extension of subscriber benefits in the future.

It is to be emphasized that at the present time any medical-service plan must and should be to a certain degree experimental, if such a voluntary program is eventually to achieve any degree of success. This implies a readiness to change and adapt specific details in the light of experience accumulated as we go along. It is in this spirit that your committee has worked and will continue to work in the development of the program, and it is in this spirit that the plan should be accepted by the physicians of New Hampshire.

National Physicians' Committee

In view of the rather widespread divergence of opinion among members of the Society in regard to the program and

from 6 to 10:30 p.m. If a single infusion is given for only nine of the twenty-four hours, a slower excretion and more desirable utilization of the fluid infused may be obtained by administering more sodium chloride.

Until information pertaining to these and other factors concerned with the optimal utilization of parenterally administered nutrients is available, the prescription of the rate of infusion and composition of parenteral fluids for a given patient must reflect common sense, careful clinical observation and a tolerance indicative of an enlightened awareness of ignorance.

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understanding about it. This plan does not interfere with doctor-and-patient relation. That is, the doctor would I in his bill for whatever he feels he is worth, whatever would be. The allowance to be made is a certain indemnity, which the schedule shows. But I can't see why that should be any difference in the patient-and-doctor relation.

The Massachusetts plan has been working out satisfactorily, a lot of these plans are good. Of course, I agree that if the medical profession could take care of all of these people satisfactorily, everything would be all right; but they are not satisfied. One of the strongest organizations is the labor union, and they are in favor of governmental control of medicine.

I feel that it would be a wise thing to try this plan, because we wait until the Government takes it over, we shall be late. If we wait until incomes drop down, we shall be too late. Of course, it is a pleasure to find people able to pay their bills. But as soon as the war is over, that is going to be different.

Dr. Robinson thought that the greatest question regarding the plan was whether it would actually furnish medical care to the low-income group. These plans had not been successful in reaching a sufficient number of people to make them really a satisfactory arrangement. One real problem was the failure of proper education regarding these plans. He added that the people want something, but they lack the proper education.

Dr. Batt said that there seemed to be a demand for the plan in his town. There was one industry here, and an effort was being made to have a prepayment plan of some sort. The workers intended to organize themselves without the assistance of the medical profession, and it seemed certain that the plan adopted would be the Blue Shield. Everyone, he said, seemed to agree that some plan was necessary for the low-income brackets.

Secretary Metcalf spoke as follows:

I went to Nashua to see Dr. Rock and various other men, because there was evidently widespread opposition there, which the committee had not encountered elsewhere. I was interested in the fact that the Nashua Medical Association had presented to other counties a set of resolutions opposing the Blue Shield. I put out my neck and asked them to put me on the program, not to argue the thing pro and con but to give them the facts and information.

It seemed to me after I got started that there weren't many men there who wanted information. In fact, I was told beforehand that the Nashua group had decided to bury the Blue Shield, and the barrage was heavy. The spark that set off the reaction in Nashua has not been mentioned tonight—the financial side of the plan. The Committee had evidently not emphasized sufficiently the fact that the stipends for medical and surgical care were allowances, because many men had the idea that there was a fee schedule, and that when an allowance of \$75 for an appendectomy was stated, this meant that no one could charge more than that for the operation, no matter how wealthy the patient was. And there were also other misconceptions related to the same subject.

The law that was passed in the General Court reads as follows, in part:

No license shall be issued to any medical service corporation until evidence is furnished the insurance company that at least 50 per cent of the physicians . . . are participating.

At the present time, 47 per cent of the eligible doctors in the State of New Hampshire have signed up, and there are four counties that have not yet been thoroughly canvassed. The signatures are still coming in, and by now probably 50 per cent of the doctors have signed up to participate in the plan.

Regarding the phrase "the area in which the corporation operates," I asked the Insurance Commissioner what that meant, and he said that the area in which the corporation operates is any medical center. It might be a county, or there might be several areas in the county. In other words, Nashua was a medical area, and Manchester was a medical area. Somersworth and Dover were medical areas. This being the case, we find that most of these medical areas have already signified by their votes that they favor the Blue Shield.

However, at the present time Nashua does not want it, and there is absolutely no reason why they should take it.

Some of the areas, like Newport and Claremont, have voted eleven to one in favor of it. It seems to me that any medical area, in accordance with the spirit and the letter of the law, is entitled to go ahead with the plan. Therefore, my feeling is that the House of Delegates, which has considered the subject at three general sessions and two special sessions, has no particular reason to backfire at the present time and attempt to throw the plan out of a county. I think it is worth trying out. It may not be a success. I hope that the effect of it will be to discourage the Wagnerites by showing the people that they can have decent medical care at a price that will not tap the payroll.

Dr. D. G. Smith said that Nashua was not alone in opposing the plan, and that the majority of the physicians in Manchester were also against it. As secretary of his county society, he reported that Dr. Metcalf presented the subject very well. There was a lengthy discussion, at the conclusion of which the Society voted 28 to 7 to reject the proposal of the Blue Shield. The Nashua Medical Society had voted unanimously in opposition to the New Hampshire Physicians' Service. He said that everyone appreciated the work that the Committee on Medical Economics had done, but that it was necessary to consider the attitude of the profession as a whole. He pointed out that there were only 400 practicing physicians in New Hampshire and that many of them were in the military services. He said it had been stressed that the plan should be postponed until the 125 or 130 men now in the service could have a chance to express their wishes about it. The plan must be sold to the doctors first, and if they did not want it, how could it be sold to the rest of the people? The National Physicians' Committee had stated that 25,000,000 people were now enrolled in the plan, but according to the statistics he had just heard, the number of people favoring various state plans totaled 800,000, not 25,000,000. In addition, there were other plans, such as that of the Farm Security Administration, which had quite an enrollment.

Dr. Sycamore stated that the larger figure included all types of service—Blue Cross, commercial companies and so forth.

Dr. D. G. Smith said that the demand for the plan in this state was not great. The Massachusetts plan went into operation in July, 1942, and the demand for it was decreasing. In New Hampshire, according to Dr. Sycamore's report, the need for the Farm Security Administration Plan was going down, since the number of families covered had been materially reduced.

Dr. Robinson said that that plan went into operation when the farmer was in need of it.

policies of the National Physicians' Committee during the last year, your committee makes no statement either in support or in opposition, deeming it advisable to leave this question to the discretion of each member.

Medical-Care Program for Clients of the Farm Security Administration

Because of the present favorable economic conditions the number of families participating in the Farm Security Administration Program has been materially reduced and the number of subscribers to the medical-care program in Grafton County and Cheshire County is insufficient to provide an adequate insurance base. This plan will be discontinued when the New Hampshire Physician Service becomes a functioning corporation, and coverage of this group will be included under the latter program.

LESLIE K. SYCAMORE, *Chairman*
R. W. ROBINSON
FRANCIS H. DUBE

Dr. Mullins, for the Committee on Officers' Reports, expressed the belief that this is the most important matter to come before the Society in many years. In view of its fundamental importance, and the necessity for making a correct decision, he said that it had not been deemed wise to make any specific recommendations except that the subject should be discussed thoroughly in the light of its assets and liabilities and without personal prejudice. It was felt that it was most important to maintain a united front. He added that the members of the Society should be willing to consider the points for and against this plan calmly and dispassionately, and then try to arrive at a common understanding, that acrimonious debate and criticism would lead nowhere and that judgment should be tempered by the fact that the decision reached might influence considerably the course of medical practice in the State for years to come.

Dr. Byron then spoke as follows:

I am definitely not in favor of any such plan, and I should like to open my argument with a challenge to those who think we should adopt it. I have asked several members about it, who have stated they were in favor of it, and the only answer I get is, "Well, it's a good thing."

It seems to me that it is a plan that will affect all branches of medicine by reason of the times in which we are practicing medicine. I think that it should be based on a better reason than just that "it's a good thing."

I am wondering if we aren't just a little bit overconscious of the Wagner Act and the Wagner-Murray-Dingell Bill, and of some of the reports sponsored by the National Physicians' Committee. Some of the reports have not been enlightening. I am wondering if, in adopting such a plan, we are not going directly into the path laid for us, and if we are not going to fall into the pitfalls that we don't want to fall into. If the plan fails, certainly we have a noose around our necks, and we are going to cry out for someone to pull the rope.

The plan does not begin to provide for every workman. Let us take the average workman, getting less than \$2000 a year; we are not going to help him very much. We shall usurp the powers we have established, and eventually we are going to lead ourselves right into the arms of socialized medicine.

Dr. McQuesten said that he thought the position of the Hillsborough County Medical Society was somewhat misunderstood by some of the men. There were certain things about the Blue Shield that were not wanted, but the argument was not necessarily against those. He took the position that

this service was not necessary, and that the argument in favor of it could not be seen.

A member stated that the practice of medicine is based on sound fundamentals. Most physicians had been going along on that basis and had made satisfactory arrangements, economically speaking, with their patients. He hated to see the medical profession going into the insurance business, and to see a split on principle.

Dr. Byron said that he thought the propaganda had made the members a little overconscious, and that they were probably assuming the defensive. He saw no justification for dealing with the situation in this way or for feeling this way about it. He added that there should really be no fear over this proposition; in fact, the act had been lying idle for some time. Dr. Fishbein had been heard to say on three different occasions that it was a threat and would disappear.

Dr. Sycamore then spoke as follows:

I have been asked the reason for such a program in New Hampshire. I think there is a definite need for an extension of medical service, because of the changing type of medical practice today. The economic burden has become greater. Fifty years ago, the physician used his own skill, and that was practically all. Today, there are so many highly technical procedures in both diagnosis and treatment that medical service is much more expensive — too much so for the average low-income patient to handle; yes, and more expensive than the physician and his fee. So that there is a definite need for a better distribution of the medical care that we have available.

There is a public demand that is growing in certain labor unions. For example, they have had a poll on this question and set up a criterion that shows a great and growing interest in this question.

It has been said that we can take care of our business ourselves. I agree. The reason why the plan is being instituted now is in the first place, that although there is no need of immediate alarm about the passage of the Wagner-Murray-Dingell Bill, most medical people believe that there is going to be some distribution of medical care in the near future, if not in the exact form of the Wagner Act, then in some form or another. At least we can be that much ahead of the possibility by making a procedure available that will be suitable to us, and we shall have something to say about what will be done, and not have it forced on us, whether we like it or not.

Another reason is this: even though the economic level of workmen is fairly high at the present time, we need experience to find out the possibilities and limitations, and we need to make experiments along this line.

As we have heard, plans have changed and plans differ, and this is the time to get some experience along that line. It will be useless to try to start a plan when the Government has passed some program of socialized medicine.

Dr. Jameson spoke as follows:

This strikes me as a very important question to consider. We know that if the states do not do something toward taking care of the low-income groups, the Government will make plans that may be more radical than the ones we are now familiar with.

We know that the general public is demanding some type of prepaid medical care. A poll showed that 75 per cent of the people wanted to have some type of medical care. In the Gallup Poll, the groups that were covered were the professional and semiprofessional people, farmers and farm managers, textile workers, clerical workers, salesmen and office and kindred workers.

It is generally believed that the general public is going to submit to some type of help in the matter of medical care. It does seem as though we could take care of this group, the low-income

as to the Blue Shield, some people could afford to pay a small fee to protect their families when they were working, but they could not afford to pay the fee when they were sick. He said that the question was not whether the physicians wanted this plan, but whether the people wanted it. If there was a public demand for it, he asserted it would come out in one way or another. The plan, if operated under supervision, should work well. Naturally, he said, this was just the beginning, and there might be mistakes and flaws but after some co-operation those could be corrected. The Society had already endorsed this plan in a legal manner and had given the committee the power to go ahead and form a corporation. That had been done, and 99 per cent of the doctors in the State of New Hampshire had already subscribed to it. He did not know how the Society could retract.

Speaker Dwinell pointed out that the motion before the house was that the Blue Shield be rejected, and suggested a standing vote.

Secretary Metcalf said that there were 114 men in the military services and that a letter and all the literature on the plan had been sent to every one of them. These were sent to the men's New Hampshire addresses. Possibly some of the letters had not been forwarded, but some of them evidently were because he had received one reply. Out of the other 350 odd members who are residents of the State, he got three replies. The one reply from the soldier said that he was heartily in favor of the plan, and that when he got back into civilian life again he would thank God it was there.

Metcalf added that this physician was a member of the Hillsborough County Society.

Dr. Mullins thought that it was unfortunate that the House was voting on a negative motion. As stated in the report of the Committee on Officers' Reports, it was felt that the situation should be dealt with positively, since the Society looked to the use of Delegates for positive leadership. The Delegates, he pointed out, were the elected representatives of the Society and represented the sentiment of most of the doctors in New Hampshire. He requested that the motion be withdrawn. Dr. Dwinell then withdrew his motion. Dr. Mullins then moved for a vote approving the action of the Committee on Medical Economics and accepting the plan of the principles of the New Hampshire Physicians' Service. This motion was duly seconded. Dr. Clough said there seemed to be too much arguing on both sides to pass or shelve the motion, and suggested laying it on the table for one year. He admitted that he had many conflicting views on the subject, but was at present strongly in favor of the motion, and said that he thought there were others present who felt the same way. He suggested that the motion should be worded so that if it were defeated it could be brought up again next year.

Speaker Dwinell called for a standing vote on Dr. Mullins's motion, and the motion was carried, with 4 dissenting votes.

Dr. Sycamore said that the law required that a majority of the Board of Directors should be approved by the House of Delegates. He therefore moved that the House of Delegates approve the Board of Directors. This motion was duly seconded by Dr. Dye and was carried.

The meeting then adjourned at 11:30 p.m. until 9 a.m., May 16.

* * *

The House of Delegates reconvened at the Hotel Carpenter, Manchester, on May 16, 1944, at 9:00 a.m., with Speaker George F. Dwinell, of Manchester, presiding.

The following members answered the roll call.

The President, *ex-officio*
 The Vice-President, *ex-officio*
 The Secretary-Treasurer, *ex-officio*
 P. R. Hoyt, Laconia
 Richard W. Robinson, Laconia
 W. J. Paul Dye, Wolfeboro
 Francis J. C. Dube, Center Ossipee
 Albert C. Johnston, Keene
 Richard Batt, Berlin
 Arthur B. Sharples, Groveton
 Leslie K. Sycamore, Hanover
 Howard N. Kingsford, Hanover
 Donald M. Clark, Peterborough
 R. E. Byron, Manchester
 Deering G. Smith, Nashua
 Clinton R. Mullins, Concord
 William P. Clough, Jr., New London
 Gerard Gaudrault, Concord
 Harry B. Carpenter, Portsmouth
 Fred Fernald, Nottingham
 Roland J. Bennett, Dover
 George G. McGregor, Durham
 Donald G. Moriarty, Newport
 Emery S. Fitch, Claremont (alternate for B. Read Lewin)
 George C. Wilkins, Manchester (alternate for Stillman G. Davis)
 Dr. Henry O. Smith, Hudson

Dr. W. J. Paul Dye, reporting for the Committee on Nominations, proposed three men for president: Fred Fernald, Nottingham; F. E. Wilder, Whitefield; and Cleon W. Colby, Exeter.

Dr. Dye then pointed out that there were two candidates for president from the same county, which was unconstitutional, and requested another nomination in place of Dr. Colby. The name of John Hunter, of Dover, was proposed and was added to the list of nominations for president.

On written ballot, Dr. Fred Fernald, of Nottingham, was elected president.

Dr. Dye then proposed three men for vice-president: John F. Gile, Hanover; Robert W. Holmes, Keene; and Edward C. Batchelder, Dover.

On written ballot, Dr. Gile was elected vice-president.

Dr. Dye then read the rest of the slate, as follows:

Dr. D. G. Smith read a passage from the report of the Board of Trustees of the American Medical Association relating to this subject, and then continued:

The American Medical Association has been urging these plans since 1943, but they have been watching them in the various states, trying to see what the best solution of the problem is. I don't believe it has yet been found. I don't believe this plan will help the low-income groups.

The question of payroll deductions will come up, and some companies will try to take care of their employees. But the employees in some places are quite upset because of the 20 per cent deductible income tax, and the social security, unemployment, Blue Cross and a lot of other deductions. Some even have deductions for life insurance, some for health and accident insurance. Whether or not employees will stand another deduction is a question.

The launching of the plan, in my estimation, is an admission of the need for it in New Hampshire. We take care of the indigent. If there is necessity for launching the Blue Shield at the present time and taking care of the medically indigent, that is one thing, and that is an argument for the Wagner Act and state medicine — in other words, it admits that the people in New Hampshire haven't been doing a good job; that there is a need for such a plan.

It was brought out in the Nashua discussions that we should not have the Society going into the insurance business. Private insurance companies are already selling insurance and taking care of the cost of medical care.

In closing, let me say that I think we should be careful in launching the boat; we should have it all built and solid, and we should have it in a place where we can launch it. It does not seem to me that we should launch the boat at this time.

Dr. Smith then moved that the New Hampshire Physicians' Service be not initiated at this time.

A member asked what the effect of the motion would be if it were carried, since he understood that the corporation had been legally formed.

Speaker Dwinell said that the people who had already accepted this plan are entitled to its service and could not be stopped by any vote.

Dr. Sycamore said he did not see how a few dissenters could presume to ask the House of Delegates to tell the members of eight counties who have already accepted the program that they should not do it.

Speaker Dwinell mentioned that he had heard no one say anything against the Blue Cross. If that had been so successful and had helped people out, why was not the Blue Shield going to help them out, too?

Dr. Robinson said that if criticism of the Blue Cross was wanted, it could be found in the records of five, six and seven years ago.

A member asked whether it was the general consensus that the Blue Shield was mainly desired as a protection against the possibility of socialized medicine.

Speaker Dwinell said that this was one reason why it was wanted.

A member suggested that the larger sections of the country that could not possibly finance any prepayment plan had been overlooked. He was referring to some of the places in the South.

Speaker Dwinell said that the plan was not intended to take care of the indigent patients who

would always be taken care of by the town or county, but was for those who had enough, but not save it.

Dr. Wilkins took exception to Dr. Smith's statement that the plan could not be undertaken until all the doctors were in favor of it, pointing out some developments in medicine had become real not because the doctors demanded them but because the public did. As examples he cited the cancer program in New Hampshire, which was actually initiated by laymen because they were interested in taking care of indigent cancer patients, and brought to the attention of the Legislature because the medical men were consulted, and the tuberculosis program, which was brought about by a lay group, the New Hampshire Tuberculosis Association and not by the medical profession. When the Blue Cross was first started, he said, the Eliot Hospital was the only hospital that agreed to it and subscribed to its provisions, and many of the other hospitals fought against it. Today, they were with it. As Dr. Robinson had said, when the Blue Cross was first introduced, the same objections and the same arguments were brought up against it as were being brought against the Blue Shield. When it proved a success, and so would the Blue Shield. This House of Delegates, he continued, had discussed this matter for three years. The committee had done an outstanding and forward-looking job and had brought something to the Society that was worth while. He said the plan ought not to be turned down, but should be given an opportunity to prove its worth. Medicine was going to be practiced differently, and all must accept it. This was one of the ways in which it would be practiced. The people, he asserted, want something to cover their unusual medical expenses; otherwise, the Government will take over this matter.

Dr. Fitch was appointed as alternate delegate in the place of Dr. Lewin, who had had to leave the meeting, and spoke as follows:

I should like to express myself in opposition to Dr. Smith's motion. I think that we should go on record in regard to this insurance question now. It would be too bad to lay it on the table for another year.

Dr. Wilkins has well expressed what I have in mind, namely, that the public is ready for this program and that they are looking for the medical profession to carry it through. It has been pretty well publicized, and the public wants to see it adopted.

In Claremont, the Sullivan Machinery Company adopted the Metropolitan plan of insurance, whereby employees pay a part of the premium and the company pays the balance, and it is very well accepted. The employees all carry private insurance.

Dr. Dye said that doctors as individuals would all like to continue practicing the way they are now doing, and felt that they had done a good job. The medical standards he said were better in this country than anywhere else in the world. Nevertheless, he added, the Wagner Bill was passed, and there is still a demand by many groups for medical insurance and medical practice.

the American Medical Association than did the of the delegates.

Dr. Smith said that the allotment of delegates to various states was based on the number of members in the state medical society — possibly one delegate to every nine hundred members, with the proviso that each state was to have at least one delegate.

He said he did not see the point of the resolution suggesting that each state should have a minimum of two delegates since this would make the membership undemocratic, the representation not being

according to the number of members. He moved that the matter be tabled, since it required no action by the House. This motion was duly seconded and carried.

Dr. Clark proposed a vote of thanks to the Manchester doctors for their cordial hospitality, and moved that next year the meeting of the House of Delegates be held in Manchester. This motion was duly seconded and was carried.

The second and final meeting of the House of Delegates was adjourned at 9:45 a.m.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30431

PRESENTATION OF CASE

First admission. A sixty-year-old woman was admitted to the hospital because of swollen joints.

The patient had had the usual childhood diseases, including measles, diphtheria, pertussis and scarlet fever. At nine years of age she had "St. Vitus dance." She was subsequently in good health, but at the age of twenty-two she had pain, swelling and tenderness in the left elbow for a short period. The following year, thirty-seven years before entry, and immediately following the birth of her second child, she developed migratory joint involvement, with pain, redness, tenderness and swelling lasting for six months. She was then asymptomatic until twenty-three years prior to entry, when following the birth of her fifth child, she again developed migratory joint pains. At that time a presystolic murmur and thrill were heard, as well as a loud apical first sound. The joint pains disappeared in two or three weeks. She was otherwise symptom free until two years prior to entry, when she had palpitation and dyspnea on exertion and was put on digitalis for several months. Four months before entry she developed sore throat, headache and general malaise, which persisted despite bed rest until two weeks before admission, at which time she experienced pain and swelling of the first and second metacarpophalangeal joints and the left ankle, as well as persistent pain and stiffness low in the back. She had some dyspnea on exertion but no fever.

*On leave of absence.

Physical examination showed a well-developed, well-nourished woman lying flat in bed and in no discomfort. There was slight edema of the left ankle. The thyroid gland was enlarged and showed a small tender nodule measuring 2 by 2 cm. in the left lobe. The left border of cardiac dullness was 10 cm. to the left of the midline. The sounds were of fairly good quality. There were apical systolic and diastolic murmurs, and a diastolic thrill. The pulmonary second sound was greater than the aortic. The lungs were clear. The abdomen was normal. The second metacarpophalangeal joints of both hands were swollen, red and extremely tender. Pain and tenderness were elicited on motion of the knees and ankles.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 96, and the respirations 20.

Examination of the blood showed a red-cell count of 4,610,000, with 90 per cent hemoglobin. The white-cell count was 6800. The urine and stools were normal. The uric acid was 2.1 gm. per 100 cc., and the sedimentation rate 1.21 mm. per minute. An electrocardiogram showed normal rhythm, with a rate of 85, a PR interval of 0.28 second, slight slurring of the QRS complexes, normal T waves and slight left-axis deviation. The basal metabolic rate was +39 per cent.

X-ray studies of the chest showed dense dullness at the right apex, with mottling below it. The right lung field was smaller than the left, especially at the apex. The heart was enlarged to the left and down.

The patient was put to bed. Hot compresses were applied to the hands and 0.65 gm. (10 gr.) of aspirin was administered daily. She felt much better and by the end of the first hospital week was symptom free. The sedimentation rate ranged from 1 to 2 mm. per minute, with a final drop to 1.1 mm. per minute on the thirtieth hospital day. On that day an electrocardiogram showed a rate of 85, with a PR interval of 0.22 second. She was discharged at the end of the fifth hospital week.

Final admission (nine years later). Following discharge the patient apparently remained well and able to work every other day until about four years later (five years before entry), when she was seen in

Secretary-Treasurer: Carleton R. Metcalf.
Councillors:

(Two elected annually for five years)

	TERM EXPIRES
Henry H. Amsden, Merrimack County	1945
Timothy F. Rock, Hillsborough County	1945
Cleon W. Colby, Rockingham County	1946
John A. Hunter, Strafford County	1946
Richard E. Wilder, Coos County	1947
W. J. Paul Dye, Carroll County	1947
Clifton S. Abbott, Belknap County	1948
Arthur W. Burnham, Grafton County	1948
Walter H. Lacey, Cheshire County	1949
Emery M. Fitch, Sullivan County	1949
<i>Trustees:</i>	
George C. Wilkins, Manchester	1945
Howard N. Kingsford, Hanover	1946
Samuel T. Ladd, Portsmouth	1947
Henry O. Smith, Hudson, Trustee Emeritus	

Speaker of House of Delegates: Ralph W. Tuttle, Wolfeboro.
Vice-Speaker of House of Delegates: Deering G. Smith, Nashua.
Delegate to A. M. A. 1944-45: Deering G. Smith, Nashua.
Alternate Delegate, 1944-45: Emery M. Fitch, Claremont.
Necrologist: Henry H. Amsden, Concord.

STANDING COMMITTEES

Advisory Committee on Jurisprudence: Clifton S. Abbott, Belknap County; W. J. Paul Dye, Carroll County; John J. Brosnahan, Cheshire County; Richard E. Wilder, Coos County; John F. Gile, Grafton County; David W. Parker, Hillsborough County; Robert J. Graves, Merrimack County; Samuel T. Ladd, Rockingham County; Jeremiah J. Morin, Strafford County; Henry C. Sanders, Jr., Sullivan County; Carleton R. Metcalf, Concord, Chairman.

Amendments to Constitution and By-laws: W. J. Paul Dye, Frederick S. Gray, Ralph N. Jones.

Child Health: Colin C. Stewart, Jr., B. Read Lewin, Franklin N. Rogers.

Control of Cancer: George C. Wilkins, Ralph E. Miller, George F. Dwinell.

Maternity and Infancy: Robert O. Blood, Benjamin P. Burpee, Marion Fairfield.

Medical Economics: Leslie K. Sycamore, Richard W. Robinson, Francis J. C. Dube.

Medical Education and Hospitals: John P. Bowler, James W. Jameson, Herbert L. Taylor.

Medical Preparedness: Deering G. Smith, Ezra A. Jones, Carleton R. Metcalf.

Mental Hygiene: Benjamin W. Baker, John B. McKenna, Simon Stone.

OPA Assistance: Charles H. Parsons, Alexander Barbeau, Philip McQuesten.

Public Health: Harris E. Powers, Anthony E. Peters, Clinton R. Mullins.

Public Relations: The President, the Vice-President, the Secretary-Treasurer, Robert J. Graves, Joseph N. Friborg.
Publication: Carleton R. Metcalf, John F. Gile, Emery M. Fitch.

Scientific Work: Carleton R. Metcalf, Frederic P. Scribner, Sven Gundersen.

Tuberculosis: Robert B. Kerr, Richard C. Batt, Charles H. Parsons.

The Secretary was instructed to cast one ballot for the remainder of officers and committee members, as nominated; this was done, and all were declared duly elected.

Report of the Committee on Memorials and Communications

The committee has two matters to take up. We have one communication from the Office of Price Administration in connection with the rationing of special food for the sick people. The OPA wants the Society to appoint a committee to see that the sick person really is sick, and really needs special food rations. They want to see that the sick people have what they should have, but they want to understand that the person really needs it.

The committee is in favor of this proposition from the OPA and recommends the following committee: C. H. Parsons, Concord; Alexander Barbeau, Manchester, and Philip McQuesten, Nashua.

I also have a communication from the Medical Association of Southern California relative to the House of Delegates of the American Medical Association. It seems that the minimum number of delegates from a state is one, the more populous states having twenty or more delegates. The recommendation from the Southern California Medical Association is as follows:

BE IT RESOLVED, That the House of Delegates of the Southern California Medical Association petition the House of Delegates of the American Medical Association to amend its constitution and by-laws so that the minimum number of delegates to which each constituent organization is entitled shall be two, instead of one.

In other words, each state would have at least two delegates to the American Medical Association instead of one.

Dr. McGregor did not understand how the OPA plan was going to function. He asked whether, for example, if he had a diabetic patient he must consult somebody in Nashua.

Dr. Kingsford stated that the OPA wanted a committee appointed by the Society to which the OPA could turn if the demand was not authentic or seemed unreasonable.

Dr. McGregor asked if the committee would examine the records at Nashua to see if he was right.

Dr. Kingsford said that he did not understand it in that way. He explained that the OPA had many applications from people who were not licensed doctors, and needed someone to check them. He did not believe that the OPA sought to question anything that a regular physician did.

Dr. Robinson said that this was being done, and that prescriptions of physicians in regard to food thought necessary in particular cases were being questioned. He reported that he prescribed a diet for a patient with a severe nephrosis, and that the OPA wrote to him saying that it could allow his protein diets only for tuberculosis.

Dr. Kingsford said that the Society should have a committee to back up its members.

Secretary Metcalf said it was just this type of case that the OPA wanted to refer to a group of three doctors. He said that there were relatively few cases where the matter came into question at all, but that every once in a while the OPA got a case in which it did not know whether to say "yes" or "no." It would like some responsible committee from the New Hampshire Medical Society to which it could refer such a case for advice, not wanting to pass on it themselves for fear that whatever the said would be unjust. According to the OPA there were only two or three such cases a month.

Dr. Sycamore moved that the committee, if named, be constituted to co-operate with the OPA. This motion was duly seconded and was carried.

Speaker Dwinell said that the second part of the committee report should be discussed by Dr. D. Smith, since he knew more about the constitution.

olic murmur was very faint. The extremities were cold. There was ptosis of the right eye, and both pupils were dilated and fixed to light. The right arm seemed limper than the left. No marked changes in reflexes were noted. The blood pressure was 110 systolic, 70 diastolic. The temperature was from 102 to 99°F. The radial pulse was 80. An electrocardiogram revealed auricular fibrillation with a rate of 120 and some change from the previous tracings, in that T₂ as well as T₁ had become inverted, with depression of ST₄ and inversion of T₄. On the following day the right arm became cold, pulseless, blue and flaccid. The right leg was weaker than the left. The tendon reflexes were equal. The blood pressure was 156 systolic, 88 diastolic, in the left arm. There were signs of consolidation in the left lung base. Breathing became stertorous, the coma deepened, the temperature rose to 102°F., and the patient died on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. T. DUCKETT JONES: This case is long on paper and in years. At a young age the patient's rheumatic story began with Sydenham's chorea and followed a characteristic pattern in that heart disease did not develop until many years later after definite attack of rheumatic fever. We have found that, in a group of reasonably well-followed chorea patients, the incidence of heart disease without other manifestations of rheumatic fever is extremely low, not over 18 per cent, after a period of eight or ten years. The incidence of heart disease in the total chorea group (including other manifestations of rheumatic fever) is about 50 per cent, as opposed to 70 per cent or more in rheumatic-fever patients without chorea.

The joint involvement after the birth of her second child seems characteristic of rheumatic fever. In our experience, patients developing rheumatic fever within three or four weeks of the termination of pregnancy have usually had active rheumatic fever in the recent past, that is, within two or three years of the pregnancy. In this case, rheumatic fever occurred one year prior to the episode after the second pregnancy. No information is given relative to any relation between the first pregnancy and the initial attack of rheumatic fever. Fourteen years elapsed, however, between the second and third clinical attacks of rheumatic fever, and the latter followed the fifth pregnancy. Since heart disease was noted initially during this attack, one wonders if mild or subclinical rheumatic fever may not have occurred at some time during the latter part of the fourteen-year period. This would help explain the interval between the two early attacks of rheumatic fever and the finding of mitral stenosis during the third attack many years later. Since presystolic murmurs are easily heard late in pregnancy, it seems probable that, if present, it would have been heard during the third or fourth preg-

nancies. Where there is definite evidence of rheumatic fever even without heart disease we advise the patient not to become pregnant until two or three years after the termination of the active disease.

In view of the history and findings on the first admission, we are forced to accept the fact that, at the age of sixty, after an interval of twenty-three years without clinical attacks of rheumatic fever, there was a rather characteristic recurrence of rheumatic fever. This is a rather unusual story, in fact, I believe that it is rare. It did follow a definite story of sore throat, and one wonders if intimate exposure to the hemolytic-streptococcus infections of her children and later of her grandchildren may not help explain the pattern of illnesses. There were apical systolic and diastolic murmurs and a diastolic thrill. One would presume that there was a presystolic phase (crescendo) of the diastolic murmur and that the diagnosis of mitral stenosis was justified. The sedimentation rate and the electrocardiographic findings are entirely in keeping with active rheumatic fever.

The high metabolic rate was probably due to the active disease rather than to any effect of the small nodule in the thyroid gland.

We do not know how long the active rheumatic fever continued. This adult of sixty certainly had the disease for a few months: she had it for some time prior to hospital admission and it continued at the time of discharge, as shown by the sedimentation rate and the long PR interval.

On second admission she gave a story of hemoptysis. There are several causes of hemoptysis in a rheumatic-fever patient. On rare occasions, one sees it in young people even without mitral stenosis. During active rheumatic fever, it occurs but is rare. More frequently it is associated with acute, left-sided failure in patients with old and severe rheumatic heart disease, especially mitral stenosis. This patient, however, did not have such an acute episode. There is a reasonably large group of patients in whom hemoptysis occurs purely on the basis of mechanical failure, without evidence of active rheumatic fever. I recall a few patients being followed in the Out Patient Department who repeatedly came back to the Emergency Ward or at times were admitted to the hospital because of repeated hemoptyses and who had absolutely normal laboratory findings. One wonders if this is the result of pulmonary-artery disease comparable with that reported by Parker and Weiss¹ in which there were changes in the pulmonary vessels of mitral-stenosis patients similar to those seen throughout the body in patients with arteriolar sclerosis. These authors call attention to the similarity of the changes in vessels seen in nephrosclerosis. To me it seems likelier that the majority of these patients have either small pulmonary infarcts or pulmonary thrombi, rather than actual arterial disease, as the

the Emergency Ward following repeated episodes of hemoptysis over a period of twenty-four hours, amounting in all to about half a cupful of blood. She had had no chest pain, fever or chills. Examination showed the lungs to be clear, with bronchovesicular breath sounds in the right paravertebral region posteriorly. The left border of cardiac dullness was 8.5 cm. to the left in the sixth space. An apical, rumbling, crescendo, presystolic murmur was heard. The blood pressure was 180 systolic, 90 diastolic. The temperature was 99°F., the pulse 72, and the respirations 20. X-ray examination of the chest showed definite increase in the size of the heart since the previous examination. The enlargement was on both sides, and there was prominence of the pulmonary conus. The hilar shadows were slightly increased, and there was a marked increase of the linear markings, with areas of increased density scattered throughout both lung fields. She was advised to take it easy and rest in bed and to return in one month.

She was not seen for the next five years, except for the treatment of varicose ulcers of the leg, which healed slowly, but was apparently asymptomatic until five months before the final admission, when she noted moderate dyspnea which came on when she was out of doors or climbing but not doing strenuous work around the house. She had had occasional attacks of palpitation and felt extremely nervous. She experienced difficulty in swallowing, consisting of a sensation of discomfort, which extended over the anterior surface of the neck, and occasionally felt as if the food stuck. Examination in the Out Patient Department three months before entry revealed essentially the same findings as before. The blood pressure was 198 systolic, 118 diastolic. The pulse was regular at 80. The sedimentation rate was 0.74 mm. per minute, and the hematocrit 43. She was advised to return for admission, but refused. The dyspnea progressed in severity.

Three days before entry the patient developed weakness and general malaise. She became increasingly dyspneic, anorexic and cyanotic. Shortly before admission she experienced a smothering sensation, with marked dyspnea and orthopnea. She had no peripheral edema, chest pain, chills or fever. She was referred to the hospital after her physician had been unable to control the attack with morphine.

Physical examination showed a well-nourished, dyspneic, cyanotic woman. The neck veins were slightly distended. The lungs were resonant. There were decreased breath sounds and many moist rales in both lung fields posteriorly. The left border of cardiac dullness was 10 cm. to the left of the midline in the fifth space. There was auricular fibrillation at a rate of 120. The heart sounds were weak. A systolic murmur and a rumbling mid-diastolic murmur were heard at the apex along the left sternal border. The liver edge was felt 2 cm. below the right

costal margin. A healed varicose ulcer and st dermatitis were present on the left leg, but there was no frank pitting edema.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 99.2°F., the pulse 120, and respirations 28.

Examination of the blood showed a red-cell count of 3,960,000, with 12.8 gm. of hemoglobin. The white-cell count was 10,400, with 85 per cent neutrophils. The urine gave a specific gravity of 1.020 and a + test for albumin; occasional red, white epithelial cells were found in the sediment. The nonprotein nitrogen was 28.5 mg. per 100 cc., the serum protein 6 gm.

X-ray films of the chest showed marked enlargement of the heart, the left border almost touching the axilla. The left main bronchus seemed to be elevated, probably owing to enlargement of the auricle. The hilar vessels were slightly engorged. There were linear areas of increased density extending upward from the hilar vessels to the apices, marked on the right.

The patient was given oxygen and 4 cc. of Cedonid intravenously, followed by 0.2 gm. (3 gr.) digitalis and 2 gm. (30 gr.) of ammonium chloride by mouth, with marked improvement. On the second hospital day the pulse rate fell to 56, with a subsequent rise to 80 within a few hours, and then to 100, where it remained. She was given the usual diuretic regime of ammonium chloride three times a week, with Mercupurin. An electrocardiogram on the second hospital day showed auricular fibrillation with a rate of 70. T_1 and T_2 were low, ST_1 and ST_2 depressed, and T_3 flat and T_4 diphase. There was left-axis deviation. The urinary output on the second hospital day rose to 2250 cc. on a fluid intake of 1000 cc. and thereafter equaled the intake. The temperature varied between 100 and 101°F. The white-cell count ranged from 7500 to 10,500.

On the third hospital day the patient was awakened from sleep by a sudden, severe, precordial pain which was worse on deep breathing. Examination showed fine crackling rales at both lung bases. The heart was the same as before. There was tenderness in the left calf. Homans's sign was negative. The blood pressure was 180 systolic, 90 diastolic. The pulse was 100, and the respirations 30 and labored. An electrocardiogram revealed auricular fibrillation with a rate of 100. T_1 was inverted, ST_2 and ST_3 deeply depressed, T_2 upright, and T_3 diphase; Lead 4 was normal. X-ray studies of the chest showed no change. A bilateral femoral ligation was performed. The pain apparently disappeared but the patient continued to run a low-grade fever and was moderately dyspneic and orthopneic. On the seventh hospital day she became rather suddenly unresponsive. Examination showed a marked change in the heart sounds, which were not tic-tac in quality. The systolic murmur could not be heard. The di-

The chances of this are rare. I believe that one would be safer to stick to rheumatic heart disease as the basis of her demise.

I presume that it is unlikely that she had active rheumatic fever at the time of death. The usual pattern of fatal progressive rheumatic heart disease results in death at an earlier age, usually fifteen or twenty years after the initial attack. I should say that there is little chance that she had Aschoff bodies; this is possible, however, since she had rheumatic fever as late as the age of sixty. I do not believe that it is necessary to predicate active rheumatic fever during her terminal illness. We know that in old people the onset of auricular fibrillation is not necessarily associated with active rheumatic fever, but it is frequent in children and young adults.

I explain the entire picture on the basis of rheumatic heart disease with extensive thrombi in the heart. There may have been some evidence of old pulmonary infarcts or thrombi. Emboli were present in the brain and the right arm at the end, and probably in the coronary arteries. The terminal coronary accident may have been on this basis rather than due to straight arteriosclerosis.

DR. LAURENCE L. ROBBINS: These films are not particularly helpful. They were taken at the time of the final admission. The patient apparently stayed out of the hospital long enough so that the early films were destroyed, and we have no way of following the course of the disease.

There is not much question about the cardiac enlargement. The left ventricle and left auricle are apparently enlarged, and there is some elevation of the bronchus with widening of the carina. I do not see anything that suggests recent infarction, at least within the lung. There is an old process in the right upper lobe to which some consideration ought to be given; it looks now like an old, tuberculous, bronchiectatic affair. There is one shadow in the right lower lung field that possibly represents an old healed infarct; it is simply a scar.

DR. JONES: When was this film taken?

DR. ROBBINS: Two days before she died.

DR. CONGER WILLIAMS: The electrocardiographic changes are not at all diagnostic of a coronary episode. One often sees quite a marked change in the terminal stages. I do not believe that one can conclude that these changes were the result of infarction. T-wave changes are present, but they are not sufficiently clear cut to be sure about them.

DR. CASTLEMAN: The electrocardiogram taken immediately after the episode was interpreted as being consistent with a recent anterior occlusion.

DR. WILLIAMS: It is a possibility, but I do not believe that one can say that it is diagnostic.

CLINICAL DIAGNOSES

Rheumatic heart disease, with mitral stenosis and regurgitation.
Auricular fibrillation.

Congestive heart failure.
Acute pulmonary edema.
Pulmonary embolus?
Cerebral embolus.
Pneumonia, left lower lobe.

DR. JONES'S DIAGNOSES

Rheumatic heart disease.
Mitral stenosis.
Auricular fibrillation.
Congestive heart failure.
Old pulmonary infarcts or emboli?
Coronary closure (? embolic).

ANATOMICAL DIAGNOSES

Rheumatic heart disease.
Endocarditis, subacute and chronic, rheumatic: mitral and aortic valves, with stenosis of mitral valve.
Atheromatosis of aorta and coronary arteries, marked.
Thrombosis of anterior descending branch of left coronary artery.
Myocardial infarction: anterior wall of left ventricle and anterior portion of septum.
Cardiac hypertrophy.
Mural thrombus: left auricle.
Embolism of axillary artery, with early gangrene: right forearm and hand.
Bronchopneumonia: right lower lobe.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed an enlarged heart (480 gm.), but one not so large as might have been expected in a patient who had had heart disease for many years. There was a mitral stenosis of moderate degree, and slight aortic disease. We could not get two fingers into the mitral valve. On the mitral valve there were small, fairly firm vegetations measuring 0.5 to 1 mm. in diameter, and above there was a mural thrombus in the left auricle. On microscopic section the valve showed an active rheumatic process; there was no evidence of palisading, but a lot of cellular infiltration and granulation tissue. The lesion was definitely older than four years, thus indicating that there had been mild rheumatic activity most of the time. The myocardium showed no Aschoff nodules. There were a few suggestive areas, and perhaps with more sections we might have been able to find a few. In the anterior wall of the left ventricle we found hemorrhagic discoloration; there was no mural thrombus over it, but it appeared softer than the rest of the myocardium and our sections show that it was a recent infarction. The coronary arteries were moderately sclerotic and calcified, and in the descending branch on the left we found evidence of recent thrombosis. I am fairly certain that it was a thrombus and not an embolus, because I do not believe

basis of their hemoptysis. Such patterns are variable and difficult to be sure of unless one has enough evidence to make a diagnosis of pulmonary infarction, or unless acute pulmonary edema exists.

No electrocardiogram was made at the time of the second admission. It might have helped in delineating the cause of the hemoptysis.

I presume that this patient had difficulty in swallowing—a sensation of discomfort and so forth—on the basis of esophageal distortion, which is frequent in extensive rheumatic heart disease with left auricular enlargement. There is some x-ray evidence that she had such a syndrome.

"The blood pressure was 198 systolic, 118 diastolic." This is the first time that there was increase in the diastolic pressure, and it may be significant.

A paroxysmal arrhythmia may have caused some of her trouble but there is no clear-cut indication of it.

At the time of the last admission she was sixty-nine, a ripe age for a patient with rheumatic heart disease. Heart disease was known to have been present for thirty-one years, and she lived for sixty years after chorea and for forty-seven years after the first clinical attack of rheumatic fever. At sixty-nine she had an acute episode that was severe enough to bring her to the hospital. Despite the frequent admonishment to return, she was not regular in following advice and came in only when she was distressingly in need of help.

At that time, so far as we have proof, there had been no frank active rheumatic fever since the age of sixty, although it is possible that she had active rheumatic fever at the age of sixty-four. The chief features of her difficulties at the age of sixty-four, however, were more in keeping with a heart that is failing than with rheumatic fever with failure on the basis of the active infection. I know that Dr. Castleman wants me to commit myself whether or not she had active rheumatic fever at the end, in addition to other diagnoses.

For the first time she was fibrillating, many years after known mitral stenosis.

The later findings may be a red herring in view of the developments. I might point out here that she had good basis for a thrombophlebitis, which has to be taken into consideration. She had a distinct drop in blood pressure, which usually happens at the onset of fibrillation. So long as her pressure remained elevated she did reasonably well. This has been pointed out by Dr. S. A. Levine² as being usual in patients with mitral stenosis. The question whether or not she had a pulmonary infarct at that time is pertinent. I presume that this was probable and that it accounted for the change on the third hospital day. The electrocardiogram showed partial digitalis effect. She had an acute episode with not only pain in the chest but something happening in the leg. One must think seriously of thrombophlebitis.

It is rather surprising that the blood pressure did not drop at the time of the acute episode. She did,

however, have labored respiration and pain in the left calf. It is perfectly obvious that the electrocardiogram did not suggest a pulmonary infarct as an explanation of what had happened, and it is stated that, although x-ray examination showed no change, a bilateral femoral ligation was performed. That means, of course, that they considered pulmonary infarct as being likely, with the legs as the source, which is rather surprising to me in the presence of obvious, severe, rheumatic heart disease with failure that had been present prior to the onset of the acute episode. Severe rheumatic heart disease with failure presents unusual patterns, and one does not necessarily have to explain the clinical syndrome on the basis of pulmonary infarction or on that of another possibility, namely, a coronary accident. It is obvious that there was also a cerebral infarct. There was a distinct change in electrocardiogram which I hope Dr. Williams will comment on and which to my mind—I talked this over with Dr. Wheeler before I came in—strongly suggests that there was an accident involving the coronary system. I do not see how one can avoid this interpretation under the circumstances. The questions are, Why did it occur? and, On what basis can it be explained?

In summary, here is a story of rheumatic fever and heart disease of fifty to sixty years' duration, with an obvious decrease in cardiac reserve for a period of three, four or perhaps five years. Prior to the hemoptysis, at the age of sixty-four, a definitely low cardiac reserve existed. The sudden onset of fibrillation, with the development of failure and an unexplained acute episode a few days later, was the crux of the terminal situation. The patient had pain, a drop in blood pressure, electrocardiographic changes and evidence of multiple emboli. The question is whether or not she had a typical coronary accident. She was a sixty-nine-year-old woman and certainly this might not be unexpected, and the embolic phenomena could have come from a coronary accident. I find this rather hard to believe inasmuch as she had had obvious heart disease and a distinct decrease in cardiac reserve over a period of a few years. We know that in the failing rheumatic heart, particularly in one that fibrillates, embolic phenomena are frequent. We also know that in active rheumatic fever with heart failure embolic phenomena are rare. In some patients with failing hearts and mitral stenosis, extensive intracardiac thrombi are found at autopsy. Such thrombi are often extensive and may even extend into the pulmonary tree. There has to be some explanation for the arterial phenomena, however, and it seems to me that they fit into one pattern—an elderly woman with severe heart disease, cardiac failure and embolic phenomena. I therefore suggest the rare occurrence of coronary embolism. That may not have been the mechanism, but it could perfectly well explain the coronary accident. Ordinary arteriosclerotic disease may well have been the basis, but it seems to me that

DR. BARNEY: In other words the urine contained a few red cells. The fact that it contained white cells might have been due to the fulgurations. It does not throw a great deal of light on the question.

I shall look at the x-ray films.

DR. MILFORD SCHULZ: This is the intravenous pyelogram. In this twenty-minute film you can trace the ureter down to the bladder. It is a perfectly normal ureter as regards size and course.

DR. BARNEY: The record states that the shadow of the bladder was irregular across the dome and somewhat more depressed on the right side than on the left. They are referring to this depression. One often sees that; it is of no consequence. It is often due to the fact that the lower sigmoid presses on the bladder. I cannot see, at this distance at least, any evidence of a soft-tumor shadow on the right side, unless there is something there that may be fecal matter.

On the second hospital day an operation was performed. In a case with a story like this, one would not operate on the second hospital day without doing something in the way of cystoscopic examination. It may have been done outside. Is there anything further in the record?

DR. SNIFFEN: Cystoscopy was done at the outside hospital just before entry, at which time the granular lesion was observed. He was sent in for operation.

DR. BARNEY: There are a few diagnostic possibilities to be considered. Cystoscopy at one time showed what seemed to be a papilloma at the orifice of the left ureter. When he was cystoscoped again there was an area surrounding the ureter that was red, granular and firm and covered an area 1 or 2 cm. in diameter. This does not sound like a description of a papillary tumor of the orifice of the ureter or of the bladder. If it is true that he had a papillary tumor of the left renal pelvis, one can imagine that what he had five years afterward was an implant from the papillary tumor in the pelvis into the ureter or along the course of the ureter. It may have grown more or less the length of the remaining ureter, or it may have grown just around the orifice of the ureter, or it may have been in the ureter long enough to get outside the ureter and form a tumor in the pelvic region. We not infrequently see a papillary tumor near the orifice of a ureter, or sometimes within it, and not thinking of the possibility of a kidney tumor above, we fulgurate the lesion and think that we have done our job. An intravenous or retrograde pyelogram should show whether there is a tumor in the kidney above it. If not, one is dealing with a tumor of the ureteral orifice, which is an entity in itself; whereas if there is a tumor in the kidney, it is a waste of valuable time to fulgurate the tumor at the orifice of the ureter.

I should like to know a little more about the urine from the right kidney. It is true that it secreted the dye normally, that the ureter was all right and that the kidney itself at first glance looked fairly good. It is a faint film. I should rather see a more powerful secretion of the dye. This does not look normal to me: the middle calyx is divided into two parts, and the upper calyx is slightly dilated and seems to have a somewhat different density. There is considerable density in some parts and less in other parts, and here the appearance is bifid. So I am not at all sure that something was not going on, possibly a neoplasm, in the right kidney, which would cause the hematuria. Of course, it is evident that he had, or did have, a neoplastic condition at the orifice of the left ureter. So we come down to the question whether this was a residue, so to speak, from the tumor of the renal pelvis on the left, which, after a long period of quiescence on the part of the tumor, finally started up and produced the symptoms and signs that we have been told about. If that was the case, I am surprised that there is not some mention of a mass felt by abdominal or rectal examination, or evidence in some way that there was tumor along that ureter. Nothing was apparently done to investigate the stump of the left ureter. There is nothing here to indicate that a catheter was passed into the ureter on the suspicion or chance that there might have been a papillary tumor sprinkled along its course for a greater or less distance. If that had been done we should be able to say whether there was a clean ureter with trouble at the orifice, which in itself might have been due to the tumor of the kidney pelvis that had been removed.

I also wish that a retrograde pyelogram had been done on the right kidney. We often find that an intravenous pyelogram does not give all the necessary information. There is enough suspicion aroused by the appearance of the right kidney to warrant a retrograde pyelogram. There is no evidence that this was done. Attention was focused on the orifice of the left ureter, and the patient was operated on two days after he came in.

I believe that we can rule out tuberculosis, stone and nephritis, and it therefore comes down to a tumor of the lower end of the left ureter with extrusion out into the bladder, to some growth around the ureter in that region or to some lesion in the right kidney, which, so far as I can find out, was not further investigated. My first diagnosis is residual papillary tumor of the lower end of the orifice of the left ureter and of the bladder around the orifice of the ureter. My second guess would be a pathologic lesion in the right kidney, which had not been adequately studied. The fact that the patient was operated on forty-eight hours after he came into the hospital indicates that the surgeon

that an embolus could have gone through into the area where the occlusion occurred.

There was no recent infarction of the lung, but there was evidence of old scarring in several places, such as might have occurred with previous infarction or perhaps rheumatic pneumonia. I should favor rheumatic pneumonia rather than infarction. The arterioles in many places were markedly thickened, and the media showed hypertrophy of the muscle cells.

The liver showed a mild degree of failure.

DR. JONES: Do you think it likely that, if she had not had the coronary accident, she would have followed the pattern of an early fibrillator and have gone on for many years?

DR. CASTLEMAN: She did have a mural thrombus in the left auricle.

DR. JONES: Yes; but probably all fibrillators do at the onset. They need not be extensive.

DR. JAMES NEIL: Were there any emboli or thrombi in the major cerebral vessels to explain the paralytic symptoms?

DR. CASTLEMAN: We have not yet examined the brain; she probably had small emboli.

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CASE 30432

PRESENTATION OF CASE

A forty-six-year-old man entered the hospital because of hematuria.

The patient had been in good health until nine years before entry, when he first noted blood in his urine. The bleeding was intermittent and painless. It would continue for two or three days and stop for one to four weeks. There were no clots. He was seen at a community hospital, where a left nephrectomy was performed for a papilloma of the left renal pelvis. Following the operation he was asymptomatic for five years, at the end of which time hematuria recurred. He was cystoscoped; and a tumor in the region of the left ureteral orifice was fulgurated. He subsequently had ten or twelve recurrences of hematuria, with repetition of the treatment. Following each treatment he was asymptomatic for two to five months. He was again cystoscoped. The left ureteral orifice and a surrounding area 1 to 2 cm. in diameter were firm, slightly red and granular; no definite papilloma was seen.

Physical examination showed a well-developed, well-nourished man in no distress. The lungs were clear. The heart was not enlarged. The sounds were of good quality and regular. A soft, blowing, Grade I aortic systolic murmur was heard, which

was transmitted to the neck. The abdomen was negative. Rectal examination revealed a small, firm, resilient, smooth, symmetrical prostate. The right and left lobes measured 2 by 2 by 2.5 cm., and the margins were sharp; the median sulcus was shallow, and the gland movable.

The blood pressure was 135 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 96, and the respirations 20.

A blood Hinton test was negative. The urine was cloudy, with a specific gravity of 1.016 and a + test for albumin; the sediment contained occasional red cells, 20 white cells and much debris per high-power field.

An intravenous pyelogram showed prompt excretion of the dye by the right kidney, which had a normal pelvis and ureter. The left kidney was absent. The bladder shadow was somewhat irregular across the dome, appearing somewhat more depressed on the right than on the left. No definite filling defect could be visualized. The bladder emptied normally. Plain films of the abdomen were negative. X-ray films of the chest were negative except for some evidence of emphysema.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. J. DELLINGER BARNEY: The initial hematuria apparently was due to the tumor of the left renal pelvis, which was relieved by nephrectomy. The strange part of it is that the patient went without symptoms for five years and then had recurrent intermittent hematuria. That again suggests a tumor, possibly in the other kidney, bladder or ureter. It might also have been due to stone in the remaining kidney or ureter or to tuberculosis, but the latter is not likely because tuberculosis is infrequently attended with gross hematuria. The abdomen was said to have been negative, which is rather important. The statement about the prostate aroused my interest because it seems to be the description of a normal prostate, both in size and consistence. It does not say so, but I suppose that nothing was found around the prostate or at the base of the bladder to suggest a mass of some kind that involved the tissues around the bladder.

The blood pressure appears to rule out the possibility of a hematuria due to nephritis. The fact that he had a history of intermittent hematuria with only occasional red cells does not mean much because the examination might have been done during the interval.

There is no mention of a urine culture, and I should like to know whether it was done.

DR. RONALD C. SNIFFEN: The culture showed colon bacilli.

DR. BARNEY: Was it bladder urine or urine from the right ureter?

DR. SNIFFEN: It does not say.

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fession, as such, and as represented by its society journals has the record, to date, of having held itself aloof from those party gyrations, which present no edifying spectacle at this stage of the administrative cycle.

Medicine, with no political axe to grind, although year by year it is growing more acutely conscious of its lack of such a weapon for defensive purposes. is increasingly in danger of becoming the victim of the ardent axemen of either party. Accustomed from time immemorial to minding its own business, and to being quite slow about it, it has been marked as a suitable subject for reform by those who specialize in minding other people's business, and in a hurry.

At this juncture, we congratulate the *New York State Journal of Medicine*, always the champion of medical autonomy, on an editorial in its October 2 issue in which it stresses the freedom of the medical profession from political alliances and entanglements. In this respect our profession, probably, comes closer to heeding the parting words of Washington than does any similar organization in the country, if not, indeed in the known world. This same editorial reaffirms the official commitment of the Medical Society of the State of New York to the proposition of voluntary medical-expense indemnity insurance.

A profession that goes so deeply into the lives and welfare of all the people can have no political affiliations; like the Red Cross, its functions are universal and above party considerations. Its very indispensability, however, to the Nation as a whole makes its activities and its ministrations a matter of concern to all people and all parties. If it cannot itself make its benefits universally available, then the attempt is bound to be made from without, and not well or wisely.

The scientific and the humane achievements of medicine have kept pace with the developments in other branches of human activity; its sociologic and economic aspects have been maturing more slowly, although they are making progress with the added desideratum of a sure footing. In Massachusetts, with the Blue Cross, the Blue Shield and now the Blue Triangle available, we are keeping well in the front of this economic progress, and ask only

THE TUMULT AND THE SHOUTING

REGULARLY every four years, in our democracy, come famine or plenty, health or pestilence, prosperity or depression, peace or war, a certain not too imposing percentage of the electorate goes to the polls; there it exercises its constitutional privilege of selecting from its nominated peers those who will arbitrate the destinies of the Nation for another forty-eight months.

Whether the choice of the voters at this regularly ordained and politically hallowed period of emotional instability is to turn the rascals out or to put the rascals in, is almost entirely a matter of the point of view, since for every vice there must be a versa. Fortunately the organized medical pro-

felt fairly sure of the situation from the previous examinations.

DR. SNIFFEN: In the absence of one kidney, does the pelvis on the other side enlarge or is it the parenchyma alone?

DR. BARNEY: More the parenchyma than the pelvis, unless there is some obstruction in the ureter, of which I see no indication in this film.

DR. SNIFFEN: Dr. Smith, you operated on this man, would you like to tell us your findings?

DR. GEORGE G. SMITH: This patient was in perfectly good health except for recurring attacks of hematuria that were due to a papillary tumor, which had recurred always in the same place. This was in the region of the left ureteral orifice. His right kidney never troubled him and was adequately sustaining life. It seemed to me that the chief thing was to get rid of the tumor of the lower left ureter, which was presumably an implant from the original papilloma of the left kidney pelvis. He had had a tumor cut off with the resectoscope in that region fairly recently; on cystoscopy the whole region of the left ureteral orifice was elevated and looked a little peculiar. I could feel nothing by bimanual examination, but it seemed to me that he should have the stump of the ureter and the adjacent bladder wall removed. That was done. The ureter was quite long, but I was able to free it to the upper end, which was well above the pelvic brim. The ureter was filled with thin purulent fluid. It was taken out without being opened, and the bladder wall was excised by an oval incision, which I think went entirely outside the indurated area. That was sewed up, and the bladder drained

by a catheter through the anterior bladder wall. The patient made an uneventful convalescence except that it took him longer to heal than we had hoped. He left the hospital on the eighteenth postoperative day.

I saw the patient yesterday, — about two months after discharge, — and he was in excellent health. The urine was infected, but he had not been on urinary antiseptics lately.

CLINICAL DIAGNOSIS

Papillary carcinoma of left ureter.

DR. BARNEY'S DIAGNOSIS

Neoplasm of left ureter, secondary to neoplasm of left renal pelvis.

ANATOMICAL DIAGNOSIS

Carcinoma (Grade IIB) of left ureter.

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: Dr. Smith removed a disk of bladder about 3 cm. in diameter. In the center was the ureteral orifice and from it arose about 18 cm. of ureter. The ureter was dilated to three or four times its normal size and contained pus. In the ureter, about 1 cm. above the vesical orifice, was a tumor measuring approximately 1 cm. in diameter that completely obstructed the lumen. Several centimeters above it there were two other small tumors. Microscopic sections showed an infiltrating carcinoma of moderate malignancy. The neoplastic cells had spread to the neighboring lymphatics but not to the resected edge of the bladder.

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MASSACHUSETTS MEDICAL SOCIETY



Although the Blue Shield is operating smoothly in the vast majority of cases, it is no different from any other undertaking, in that a few misunderstandings are bound to arise. In every such instance so far, it was the lack of information that caused the trouble.

Many participating physicians do not realize that the Blue Shield is, in effect, under separate contract with subscribers whose incomes are less than \$2500 for families and \$2000 for individuals. These "under-income" or "unlimited" subscribers, as they are called, are entitled to the benefits of their membership without any additional charge by participating physicians.

In a few cases, the failure on the part of the physician to determine whether or not a patient is a Blue Shield member has led to the following type of misunderstanding: A patient arranges with a surgeon for an operation at an agreed fee. Later, when he is well, the patient informs the surgeon for the first time that he is a Blue Shield subscriber and that he is entitled to unlimited service because of his low-income status. The surgeon is then obliged to accept the Blue Shield payment, which may or may not be as much as the agreed fee.

Although the subscribers' contract technically protects the physician in cases of this kind by specifically requiring the subscriber to identify himself as a Blue Shield member at the time arrangements are made for the operation, very poor public relations result when the physician bills the under-income subscriber for an additional charge. Participating physicians have agreed as a matter of principle that under-income subscribers should not have to pay extra charges for surgery and aftercare in the hospital.

It should be remembered, however, that the physician continues to charge his regular fee to those subscribers whose incomes are larger than the amounts stated above, and thus may quite properly

bill the over-income subscriber for the amount, if any, that his fee exceeds the Blue Shield payment.

A great deal of confusion could be avoided and public relations could be immeasurably benefited if the participating physician would simply ask each patient the following two questions: Are you a Blue Shield subscriber? If so, what is your income status? The physician would not then be working in the dark, and the arrangements concerning the fee could be made with complete understanding.

DEATHS

JOHNSON — David J. Johnson, M.D., of Boston, died October 7. He was in his seventy-second year.

Dr. Johnson received his degree from Harvard Medical School in 1897. He was a member of the American Medical Association.

His widow survives.

REEVES — Marcellus Reeves, M.D., of Boston, died October 15. He was in his eighty-second year.

Dr. Reeves received his degree from Harvard Medical School in 1890. He was a member of the American Medical Association.

His widow survives.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1944

DISEASES	RÉSUMÉ		
	SEPTEMBER 1944	SEPTEMBER 1943	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	151	121	20
Chancroid	1	*	*
Chicken pox	132	114	105
Diphtheria	14	10	9
Dog bite	824	882	918
Dysentery, bacillary	40	25	25
German measles	50	59	22
Gonorrhea	410	450	470
Granuloma inguinale	0	*	*
Lymphogranuloma venereum	3	*	*
Malaria	56	15	5
Measles	92	189	150
Meningitis, meningococcal	12	42	5
Meningitis, Pfeiffer-bacillus	0	1	0
Meningitis, pneumococcal	0	4	1
Meningitis, staphylococcal	0	1	1
Meningitis, streptococcal	0	0	1
Meningitis, other forms	1	1	1
Meningitis, undetermined	3	11	1
Mumps	224	150	144
Pneumonia, lobar	66	114	114
Salmonella infections	16	30	16
Scarlet fever	244	397	168
Syphilis	363	482	427
Tuberculosis, pulmonary	216	188	239
Tuberculosis, other forms	12	26	23
Typhoid fever	4	2	7
Undulant fever	2	2	3
Whooping cough	286	301	474

*Made reportable in December, 1943.

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941

COMMENT

Anterior poliomyelitis continued high as compared with the seven-year median for the month of September, but at a figure far below that of epidemic years.

Diphtheria continued at too high a level. Only once since 1936 has September shown more cases. It is obvious that more children must be immunized.

Bacillary dysentery ran rather high during September — higher than during any previous month this year. Moreover, this figure has been exceeded only three times by the September figures of the last eleven years.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Agawam, 1; Arlington, 1; Belmont, 1; Boston, 5; Boylston, 1; Braintree, 1; Brookline, 5; Cambridge, 2; Cheshire, 1; Chicopee, 7; Dalton, 2; Danvers, 1; Deerfield, 1; East Longmeadow, 1;

for freedom from bungling interference by any party.

The tumult and the shouting of an election year will soon die away; may it leave in high political places, as well as in the less conspicuous ranks of medical practice, the same ancient sacrifice of "a humble and a contrite heart"!

SYNTHETIC QUININE

THE sensational medical history of cinchona and its best-known alkaloid quinine¹ is being continued in our own time by the sealing off of the foremost natural source of cinchona bark when the Netherlands East Indies were seized by the Japanese early in the present war and by a great scientific achievement—the synthetic production of quinine.

The first event can be remedied by the passage of time and the successful outcome of the war. The second event can best be appreciated by reading the scholarly paper of Haggis¹ entitled "Fundamental Errors in the Early History of Cinchona." This account illustrates the extent by which the discovery and application of a remedial plant can be obscured by the past, and the painstaking labors necessary to unravel fact from fiction. Coincident with the increasing need of quinine for the treatment of malaria and the use of quinidine, another alkaloid of the cinchona bark, for cardiac treatment, the cinchona-bark industry grew. The patience and skill acquired by the Dutch in co-ordinating horticultural practice, soil science, chemistry and forest succession for the production of cinchona bark² are reflected in figures given by Taylor,³ who states that before the present war the world consumption of quinine was 722 tons annually and that before the invasion of Java, in the year 1941, the annual production was 1017 tons. In contrast to the centuries needed for the production of quinine by natural methods, the efforts of two chemists, Woodward and Doering,^{4, 5} over a period of fourteen months, have culminated in the synthetic production of quinine.

Much of the publicity attendant to this achievement gave the unfortunate impression that syn-

thetic quinine is now available and will relieve the need for other antimalarial drugs by the armed forces and that quinine is the most effective drug for prophylaxis and the production of radical cures. As a matter of fact, synthetic quinine is a scientific curiosity and is still far from being on a practical production schedule. Furthermore, the effectiveness of quinine as an antimalarial drug is far from 100 per cent. Quinine used prophylactically does not prevent infection, although it does suppress the development of clinical malaria. In treatment, an authoritative report by the League of Nations⁶ states:

The treatment of primary *P. vivax* and *P. malariae* infections with quinine in the usual doses [1 gm. daily] is followed by relapses in a proportion of individuals which may be as high as 50 per cent. . . . On the fully-developed gametocytes of *P. falciparum*, quinine has only a slight action.

An additional factor influencing the need for quinine is a recent report by the Board for the Coordination of Malarial Studies of the National Research Council,⁷ which claims that quinacrine (atabrine), when administered in proper dosages, produces results in the routine suppression and treatment of malaria that are comparable to those obtainable by the use of quinine or totaquine, one of the less highly purified derivatives of cinchona bark. In fact, the board stated: "There is convincing evidence that quinacrine not only suppresses the clinical symptoms of falciparum malaria but also cures this malignant form. The evidence of a similar curative effect of quinine is not conclusive." Unfortunately, relapses of vivax malaria are not prevented by quinacrine or quinine when a course of treatment is terminated.

All in all, it seems unlikely that the ingenuity of industrial chemists will be invoked to develop a means for the commercial production of synthetic quinine, as it was for the manufacture of penicillin. This in no way detracts from the brilliant experiments of Woodward and Doering. In fact, their method for the synthesis of quinine may eventually lead to the long-sought ideal—an antimalarial drug that is 100 per cent effective. Until such time, adequate amounts of the known antimalarial drugs and skill in their administration comprise the most potent weapon in the battle against malaria.

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PENICILLIN IN SULFONAMIDE-RESISTANT GONORRHEA*

A Review of 200 Cases

LIEUTENANT COMMANDER N. S. SCARCELLO (MC), U.S.N.R.

ST. ALBANS, LONG ISLAND, NEW YORK

ALTHOUGH penicillin was discovered in 1929 by H. Fleming,¹ its use in clinical work did not take place until 1940. In that year a group of Oxford investigators² published a paper entitled "Penicillin: A Chemotherapeutic Agent." This was followed in 1941 with another report on the practical use of penicillin.³ From then on, reports of the miraculous effect of the drug have been increasing daily. Limited supplies were insufficient for all investigators, and since penicillin was being manufactured under government supervision, it was reserved chiefly for military use.

It was early recognized that penicillin has a definite place in sulfonamide-resistant cases.^{4, 5} This was proved by tests with sulfonamide-resistant organisms and by treating sulfonamide-fast cases of gonorrhea.⁶

Permission to use penicillin at the United States Naval Hospital in St. Albans, Long Island, was given in July, 1943, by the Bureau of Medicine and Surgery. To affect the maximum utilization of the limited quantities available, it was directed that it be used in cases of sulfonamide-resistant gonorrhea. These were cases that had failed to respond to two courses of sulfonamides, each course consisting of at least 20 gm. of the drug.

PHARMACOLOGY

Penicillin is produced from the mold *Penicillium notatum*. It is supplied in sterile ampoules as a sodium salt for clinical use and appears as a yellow or light-brown amorphous powder. It is readily soluble in water and in saline and glucose solutions, and is subject to deterioration if exposed to high temperatures or even to room temperatures for an extended period of time. It is stable to light, but must be kept stored at a temperature

below 5°C. — whether in powder form or in solution. It is readily absorbed when given by the intramuscular route and more slowly when given subcutaneously, and is rapidly excreted through the urinary tract,⁷ a large part of the injected drug being lost within a few hours. This must be kept in mind to obtain the best results and to maintain a sufficient concentration of the drug within the blood stream. It must be given in sufficient doses and at frequent regular intervals, as may be required for the specific infection under treatment.

Although penicillin has a powerful bacteriostatic action,^{8, 9} it has been found to have some bactericidal action as well. It is remarkably effective in the treatment of infections produced by *Staphylococcus aureus*, pneumococci and hemolytic streptococci. In general, penicillin is not effective against gram-negative organisms. Exceptions to this rule are the gonococci and meningococci. The gonococci, especially those in the sulfonamide-resistant group, appear to be remarkably susceptible.

Penicillin has so far proved to be nontoxic.¹⁰⁻¹²

METHOD OF STUDY

This paper is a review of 200 cases of sulfonamide-resistant gonorrhea treated with penicillin, in the majority of which a sulfonamide drug had been given for at least two weeks, representing a total of 40 gm. The periods of sulfonamide therapy were as follows: in 6 cases, at least one week; in 44 cases, two weeks; in 35 cases, three weeks; in 34 cases, four weeks; in 18 cases, five weeks; in 23 cases, six weeks; in 23 cases, seven weeks; in 6 cases, eight weeks; in 4 cases, nine weeks; and in 7 cases, ten weeks.

On entry all the patients had a positive urethral or prostatic smear or culture, or both. One hundred and twenty-nine patients had a marked urethral discharge, 16 a moderate discharge, 46 a slight discharge, and 9 either a "morning tear" or a positive prostatic culture.

Using the two-glass test, the second sample was clear in approximately 75 per cent of the pa-

*From the Urological Department, United States Naval Hospital, St. Albans, Long Island.

Read at a meeting of the New England Section of the American Urological Association, Boston, April 27, 1944.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

Frammingham, 1; Fort Devens, 2; Greenfield, 1; Hadley, 1; Hampden, 3; Hancock, 1; Hanover, 1; Haverhill, 4; Holyoke, 3; Lenox, 1; Ludlow, 4; Lynn, 1; Medford, 2; Melrose, 1; Middlefield, 1; Milton, 2; Natick, 1; Newton, 2; North Adams, 1; North Reading, 1; Northampton, 1; Oxford, 1; Pembroke, 4; Pittsfield, 7; Quincy, 2; Revere, 1; Sharon, 1; Shelburne, 1; Somerville, 2; South Hadley, 1; Southampton, 1; Southbridge, 1; Springfield, 33; Watertown, 2; West Springfield, 3; Westfield, 1; Wilbraham, 1; Williamstown, 1; Worcester, 30; total, 131.

Anthrax was reported from: Somerville, 1; total, 1.

Diphtheria was reported from: Boston, 3; Chelmsford, 1; Dracut, 1; Everett, 1; Lawrence, 1; Medford, 5; New Bedford, 1; Somerville, 1; total, 14.

Dysentery, bacillary, was reported from: Boston, 5; Cambridge, 1; Everett, 1; Lawrence, 2; Lowell, 2; Malden, 5; Marblehead, 1; Saugus, 1; Wellesley, 1; Wrentham, 1; Worcester, 20; total, 40.

Encephalitis, infectious, was reported from: Auburn, 1; Lynn, 1; Methuen, 1; total, 3.

Malaria was reported from: Boston, 5; Brookline, 1; Camp Edwards, 16; Fort Devens, 10; Haverhill, 2; Natick, 1; Woburn, 1; total, 36.

Meningitis, meningococcal, was reported from: Attleboro, 1; Boston, 4; Brockton, 1; Chicopee, 1; Dedham, 1; Easthampton, 1; Leominster, 1; Malden, 1; Quincy, 1; total, 12.

Meningitis, other forms, was reported from: Somerville, 1; total, 1.

Meningitis, undetermined, was reported from: Milford, 1; Springfield, 1; Worcester, 1; total, 3.

Salmonella infections were reported from: Attleboro, 2; Boston, 1; Fall River, 3; Malden, 3; Medford, 2; Sheffield, 1; Springfield, 1; Walpole, 1; Wellesley, 2; total, 16.

Septic sore throat was reported from: Amherst, 1; Boston, 4; Marion, 1; total, 6.

Tetanus was reported from: Boston, 1; Oakham, 1; total, 2.

Trachoma was reported from: Cambridge, 1; total, 1.

Trichinosis was reported from: Chesterfield, 1; total, 1.

Typhoid fever was reported from: Chelsea, 1; Holyoke, 1; Lynnfield, 1; Worcester, 1; total, 4.

Undulant fever was reported from: Belmont, 1; Brockton, 1; total, 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	November 1	William T. Green
Lowell	November 3	Albert H. Brewster
Salem	November 6	Paul W. Hugenberger
Brockton	November 9	George W. Van Gorder
Springfield	November 15	Garry deN. Hough, Jr.
Worcester	November 17	John W. O'Meara
Pittsfield	November 20	Frank L. Slowick
Fall River	November 27	Eugene A. McCarthy
Hyannis	November 28	Paul L. Norton

NOTICES

AMERICAN FEDERATION FOR CLINICAL RESEARCH

An all-day meeting of the Eastern Section of the American Federation for Clinical Research is being planned for December 9. Investigators desiring to read papers on clinical research should submit an abstract of not over 200 words to Dr. Orville Bailey, Harvard Medical School, 25 Shattuck Street, Boston 15, before November 15. The meeting will be held in Boston and will be open to members of the medical profession.

POSTGRADUATE CLINICS IN DERMATOLOGY AND SYPHILIS

Owing to requests for postgraduate work in dermatology and syphilology, the Department of Cutaneous Diseases and Syphilis of the Boston City Hospital will conduct weekly clinics for instruction in the diagnosis and treatment of cutaneous diseases and syphilis. All physicians are invited.

Meetings will be held in the Dowling Amphitheatre on Fridays at 10:50 a.m. during the academic year. The first meeting was held October 6, when a symposium on psoriasis was conducted.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, November 2, in the classroom of the Nurses' Residence, at 7:15 p.m. Dr. Maurice Fremont Smith will speak on the subject "The Use and Misuse of Hormone Therapy." Dr. Anne Hopkins will be chairman.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, November 1 — Penicillin in Venereal Disease Dr. Oscar F. Cox.

Friday, November 3 — The Effect of Testosterone Compounds in Hyperthyroidism. Dr. Edward C. Reifstein Jr.

Wednesday, November 8 — Modern Anesthesia. Dr. Frank W. Marvin.

Friday, November 10 — Review of Electroencephalograms Made on Pratt Diagnostic Hospital Cases. Dr. John A. Abbott.

Tuesday, November 14 — Newer Diuretics Dr. Werner Lipschitz.

Wednesday, November 15 — Present-Day Treatment of Hypertension. Dr. David Ayman.

Friday, November 17 — Recent Advances in Cardiology Dr. Samuel Levine.

Wednesday, November 22 — Arterial Insufficiency in the Lower Extremities. Dr. John Homans.

Friday, November 24 — Diagnosis of Uterine Cancer by Vaginal Smear. Dr. Joe Vincent Meigs.

Wednesday, November 29 — Signs and Symptoms of Nutritional Disturbances. Motion picture film shown through the courtesy of E. R. Squibb & Sons.

On Monday mornings clinics will be given by Dr. Samuel Proger. On Saturday mornings clinics will be given by Dr. William Dameshek.

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 2

THURSDAY, NOVEMBER 2

7:15 p.m. The Use and Misuse of Hormone Therapy Dr. Maurice Fremont-Smith New England Hospital for Women and Children

FRIDAY, NOVEMBER 3

10:50 a.m. Postgraduate clinic in dermatology and syphilis Dowling Amphitheatre, Boston City Hospital

SATURDAY, NOVEMBER 4

*10:00 a.m.-12:00 m. Medical staff rounds Peter Bent Brigham Hospital

MONDAY, NOVEMBER 6

12:00 m.-1:00 p.m. Clinicopathological conference Peter Bent Brigham Hospital

TUESDAY, NOVEMBER 7

*12:15-1:15 p.m. Clinicoroentgenological conference Peter Bent Brigham Hospital

WEDNESDAY, NOVEMBER 8

*12:00 m. Clinicopathological conference Children's Hospital.
7:15 p.m. Graduate seminar in pediatrics Children's Medical Service, Massachusetts General Hospital, Amphitheatre 3A

*Open to the medical profession.

NOVEMBER 1-29. Joseph H. Pratt Diagnostic Hospital Medical conference program. Notice elsewhere on this page

NOVEMBER 2-4 Association of Military Surgeons Page XIII, issue of August 17

NOVEMBER 8 and 9. National Committee for Mental Hygiene Page 570, issue of October 19.

NOVEMBER 9. The Clinical and Roentgenological Diagnosis of Carcinoma of the Lung. Dr. Merrill Sosman Pentucket Association of Physicians 8:30 p.m., Haverhill

NOVEMBER 15. New England Oto-Laryngological Society Page 508, issue of October 5

DECEMBER 9. American Federation for Clinical Research Notice elsewhere on this page

DECEMBER 13 and JANUARY 3 to APRIL 25. Metropolitan State Hospital Page 508, issue of October 5.

(Notices continue)

10,000-Unit Group

Case 77. This case was complicated by a prostatic abscess moderate retention. The patient had received sulfonamide treatment over a period of months, along with irrigations and instillations. The first course of penicillin cleared acute symptoms and retention almost immediately. Discharge recurred 1 week later, and a second course (30,000 units) was given, with excellent results.

Case 86. The patient had received sulfonamide therapy for 3 weeks. Following the first course of penicillin, the discharge persisted and the cultures and smears remained positive. A second course (25,000 units) was given 2 weeks later, with no apparent improvement. Two weeks later a third course (50,000 units) was given with excellent results.

Case 144. The patient, a Negro, had received sulfonamide therapy for 3 weeks. The discharge persisted following the first course of penicillin, but cleared up immediately when a second course (25,000 units) was given 2 weeks later. The patient went to O.L., and on return had a discharge. A third course (50,000 units) brought a good response.

Case 165. The patient had received sulfonamide therapy for 5 weeks. The discharge persisted following the first course of penicillin, but after a second course 6 days later it cleared and the patient improved.

Case 176. The patient had received sulfonamide therapy for 5 weeks. He responded poorly to the first course of penicillin, the discharge continuing and the cultures remaining positive. A second course (25,000 units) produced excellent results.

30,000-Unit Group

Case 69. The patient had received sulfonamide therapy for 3 weeks. The discharge persisted following the first course of penicillin, and two weeks later an acute epididymitis developed. Four weeks after the first course, a second course (70,000 units) was given, with good results.

Case 74. The patient had received sulfonamide therapy for 10 weeks. The discharge persisted following the first course of penicillin. A second course was given 4 days later and had no effect, and a third was given 4 days after the second, with good results.

Case 80. The patient had received sulfonamide therapy for 10 weeks. The first course of penicillin failed to stop the discharge, and the cultures were positive, so that a second course (30,000 units) was given, with good results.

Case 171. The patient, who entered the hospital with a severe acute epididymitis, had received sulfonamide therapy for 2 weeks. He did not respond well to the first course of penicillin, and a second course (30,000 units) was given 8 days later, but the smears remained positive. A third course (25,000 units) was given 2 weeks later. Following this the cultures became negative, but the discharge recurred, and a fourth course (50,000 units) was given, with good results.

50,000-Unit Group

Case 99. The patient, a Negro, had received sulfonamide therapy for 2 weeks. The first course of penicillin resulted in negative cultures and smears, and a second course (50,000 units) 2 weeks later stopped a recurrent discharge.

Case 101. The patient had received sulfonamide therapy for 2 weeks. A second course (40,000 units) was necessary to control the profuse discharge that the first course of penicillin had failed to control.

Case 110. The patient had received sulfonamide therapy for 3 weeks. There was a recurrence of the discharge 1 week after the first course of penicillin, so that a second course (25,000 units) was given, with a good effect.

Case 123. The patient had received sulfonamide therapy for 10 days. Owing to a persistent slight discharge following the first course, a second course (25,000 units) of penicillin was administered and produced a clinical cure.

Case 135. The patient had received sulfonamide therapy for 2 weeks. The first course of penicillin produced good results, except that the patient developed a "morning drop." A second course (50,000 units) was given, with immediate good results.

Case 143. The patient had received sulfonamide therapy for 6 weeks. The cultures remained positive after the first course of penicillin. A second course (30,000 units) resulted in clinical cure.

Case 184. The patient had received sulfonamide therapy for 12 days. The discharge recurred 4 days after the first course of penicillin, and the cultures remained positive. A second course (30,000 units) given 5 days later was followed by good results.

30,000-Unit Group

Case 112. The patient, a Negro, had already been discharged clinically cured after a course of 60,000 units of penicillin. On readmission he was given sulfonamide therapy followed by 30,000 units of penicillin, with poor results. One week later a second course (25,000 units) was given, but positive cultures were obtained only after a third course (30,000 units).

Case 141. The patient, a Negro, had received sulfonamide therapy for 2 weeks. Although cultures became negative after the first course of penicillin, the discharge kept recurring, so that a second course (35,000 units) was given 3 weeks later. A third course (100,000 units) 1 week later produced good results.

COMPLICATIONS

Twenty-nine patients had complications on entry or developed them while in the hospital.

There were 3 patients with gonorrheal arthritis who received penicillin, and all had an immediate good response.

There were 4 cases of prostatic abscess, and all the patients showed an immediate good response to penicillin therapy.

Seventeen patients had an acute epididymitis on entry, and 5 developed epididymitis following penicillin. Penicillin had little or no apparent effect on this condition. All the patients required symptomatic treatment and bed rest, and the course of the epididymitis was not shortened by penicillin.

DISCUSSION

Penicillin has so far lived up to the predictions made for it, and has a definite place in the treatment of cases of sulfonamide-resistant gonorrhea.

No toxic reactions were noted in this series.

The Negro patients did not respond well to the drug, and approximately half of them required a repeat course.

Penicillin had little noticeable effect on the cases complicated by epididymitis, although immediate good results were obtained in the cases with gonorrheal arthritis and prostatic abscess.

The patients receiving initial courses of large dosage (100,000 units) required fewer repeat courses than those who were given smaller dosages and such a dosage should be used whenever possible.

Sulfonamide therapy should be continued as long as possible to keep the infection localized, even though clinical improvement is not noted. Irrigations and instillations, the cause of the majority of complications, should be avoided whenever possible.

The question of chancre should always be kept in mind, since some observers have found that

tients, which indicated that the infection, although not cured by the sulfonamide therapy, had been confined to the anterior urethra.

On entry, smears were taken in all cases and a two-glass test was done. While waiting for penicillin, and if there were no contraindications, the patients were given either sulfathiazole or sulfadiazine.

The penicillin was dissolved in sterile distilled water, 20 cc. of water to each 100,000 units. All the medication was given intramuscularly, with the buttocks being the site of choice and the injections alternated between them. At present, the patients receive five injections of 4 cc. (20,000 units) each at two-hour or three-hour intervals, with restriction of fluid, for a total of 100,000 units, this so-called "course" having been found to give the best results. Although there was an occasional complaint of soreness, this was no more than was to be expected with intramuscular injections, and was probably due to the giving of repeated injections in the same area. No complications followed this mode of administering the drug.

CLINICAL RESULTS

As is shown in Table 1, the total dosages of the initial courses varied, owing to the trial of different amounts. There were 27 cases (14 per cent) requiring two or more courses of penicillin. There were no failures, and all the cases cleared up after the second

TABLE 1. *Amounts of Penicillin Administered.*

NO OF CASES	DOSAGE OF INITIAL COURSE units	CASES REQUIRING REPEAT COURSES*	
		NO.	PERCENTAGE
18	150,000	1	6
15	120,000	0	0
63	100,000	8	13
31	75,000	5	16
15	60,000	4	27
56	50,000	7	13
2	30,000	2	100

*Repeat courses were given to patients who continued to have a discharge or a positive prostatic culture following the first course of penicillin.

or third course. The criterion followed for a so-called "clinical cure" was two negative prostatic cultures and smears. This regime was carried out so far as possible with due consideration to military exigencies and to the jeopardizing of the patient's condition.

More than 80 per cent of the patients had no visible urethral discharge twenty-four hours after the first course, but a few had a mucoid discharge for three or four days.

As shown by Table 1, the percentage of cases requiring repeat courses was less when large initial courses were given. Ninety-six patients received 100,000 or more units in the initial course, and only 9 of them (9 per cent) required repeat courses. There were 104 patients who received 80,000 or

less units, 18 of whom (17 per cent) required repeat courses.

The average number of hospital days in the series was reduced to approximately a third of that usually to be expected.

ANALYSIS OF REPEAT-COURSE CASES

In the following section, the cases requiring repeat courses are analyzed in brief reports, which are divided according to the number of units of penicillin given in the initial course.

Of the cases requiring repeat courses, 18 cleared up following the first repeat course, 7 required two repeat courses, and 2 needed three repeat courses.

150,000-Unit Group

Case 79. The patient had received sulfonamide therapy for 4 weeks, with no apparent clinical improvement. He did not respond well to the first course of penicillin. Four days after its administration, he developed an acute epididymitis, which was treated symptomatically. Discharge still persisted, so that a second course of 60,000 units was given 4 weeks after the first one, and the patient subsequently improved.

100,000-Unit Group

Case 68. The patient, a Negro, had previously received sulfonamide therapy for 5 weeks. Although the discharge cleared following the first course of penicillin, he continued to have a positive prostatic culture, so that a second course was given 3 weeks after the first, following which cultures became negative.

Case 78. The patient had received sulfonamide therapy for 6 weeks. Following the first course of penicillin (60,000 units), prostatic cultures remained positive, and a repeat course was given 10 days later. Cultures then became negative.

Case 82. The patient, a Negro, had received sulfonamide therapy for 9 weeks. Positive cultures persisted following the first course of penicillin, although clinically he appeared cured, with no discharge and a clear urine. Two weeks after the first course, a second one of 60,000 units was given, followed by a third of 100,000 units 2 weeks later, after which negative cultures were obtained.

Case 87. The patient, a Negro, had received sulfonamide therapy for 9 weeks. After the first course of penicillin the discharge ceased and the urine cleared, but the prostatic smears remained positive, and 10 days later the discharge recurred. A second course of 50,000 units was given, following which the discharge ceased and the cultures became negative.

Case 89. The patient had received sulfonamide therapy for 7 weeks. After the first course of penicillin the discharge, although slight, persisted for 1 week. A second course of 25,000 units was given and the patient became clinically cured.

Case 114. The patient had received sulfonamide therapy for 5 weeks. The discharge, although diminished, persisted after the first course of penicillin, but cleared up immediately following the administration of a second course of 25,000 units.

Case 142. The patient had received sulfonamide therapy for 7 weeks. On entry his condition was complicated by an acute epididymitis. The discharge persisted after the first course of penicillin and the cultures remained positive. A second course (25,000 units) was given, with no improvement 2 weeks later. A third course was given 1 week later, with no clinical improvement. One week later a fourth course of 50,000 units was given, and the smears and cultures became negative.

Case 167. The patient had received sulfonamide therapy for 4 weeks. A slight discharge persisted following the first course, and a second course of 25,000 units was given, with excellent results.

10,000-Unit Group

Case 77. This case was complicated by a prostatic abscess moderate retention. The patient had received sulfonamide treatment over a period of months, along with irrigation and instillations. The first course of penicillin cleared acute symptoms and retention almost immediately. Discharge recurred 1 week later, and a second course (30,000 units) was given, with excellent results.

Case 86. The patient had received sulfonamide therapy for 3 weeks. Following the first course of penicillin, the discharge persisted and the cultures and smears remained positive. A second course (25,000 units) was given 2 weeks later, with no apparent improvement. Two weeks later a third course (50,000 units) was given with excellent results.

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REFERENCES

1. Fleming, A. On antibacterial action of cultures of penicillin. A special reference to their use in isolation of *B. influenzae*. *Brit. J. Exper. Path.* 10:226-236, 1929.
2. Chain, E., Florey, H. W., Gardner, A. D., Heatley, N. G., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G. Penicillin as chemotherapeutic agent. *Lancet* 2:226-228, 1940.
3. Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., Jennings, M. A., and Florey, H. W. Further observations on penicillin. *Lancet* 2:177-188, 1941.
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Penicillin has definitely proved its worth in the treatment of such cases. It has made it possible

MAJOR ROBERT W. HYDE, M.C., A.U.S., AND STAFF SERGEANT RODERICK M. CHISHOLM, A.U.S.

wherein 60,000 consecutive selectees were examined. A great diversity of population density is represented, at its greatest in Boston and least in the areas of Cape Cod and the farming areas to the north and south of Boston. Most of the area studied is highly industrialized, with a diversity of mills and factories, but significant sectors are devoted to farming and fishing. The age range of the selectees was from eighteen to forty-four, with most of them between twenty-one and thirty-eight. All social strata were represented, and the group may be said to form a representative cross section of the male population at large.

The people of the area represented a wide variety of nationalities. A few communities were of almost pure English stock, now in the sixth and seventh generation in this country; others, particularly in the dense areas, were of almost completely foreign parentage. The first extensive immigration after colonial times was that of the Irish in the middle of the nineteenth century. Since that time numerous Italians have moved into the commercial areas of Boston and other coastal towns. The Portuguese have moved into the fishing villages of Cape Cod and into Fall

Selectees from the eastern segment of Massachusetts within thirty-five miles of the coastline were examined at the Boston Armed Forces Induction Station. The period covered was the winter, spring and summer months of 1941 and 1942,

er and New Bedford, and Russian Jews into ton's commercial and residential districts. The test proportion of the Chinese arrived here a China within the last decade. Many of the groes came from the South during the depression he 1930's. The Chinese have settled in one the densest areas of Boston, and the Negroes a moderately dense area of that city. he psychiatric examination, described else- ere,¹ was necessarily brief. Mental deficiency determined by a team of psychologists. The

studies^{2,3} the extent to which these factors are relevant to the incidence of mental disorders has been outlined. It was therefore possible to isolate the psychiatric differences that may have been due to racial or national factors from those that were apparently due to economic status or to population density.

RESULTS

Table 1 shows the variation of comparative rejection rates for the major mental disorders found

TABLE 1. *Relation of Percentage Rejected for All Major Psychiatric Causes to the Predominant Nationality of the Community.*

NATIONALITY	NO EXAMINED	REJECTION RATE	POPULATION DENSITY	SOCIOECONOMIC LEVEL
		%		
Negro.....	1212*	37.2	High	F—
Chinese.....	322*	31.6	High	F—
Italian.....	3472	13.7	Varied	E
Irish.....	2440	12.8	High	F
Portuguese.....	2085	10.4	Medium	E
Jewish.....	1869	9.4	Medium	D
Old American.....	1640	5.7	Low	B

*Not community but individual figures.

ost important causes of psychiatric rejection are mental deficiency, psychopathic personality, chronic alcoholism, psychoneurosis and psychoses. is with these major disorders that this study concerned.

The number from each community disqualified or each of these mental defects was ascertained. selectees are grouped in specific communities by selective Service boards. Each board represents either a city ward in a large city, part of a small city, a large town or several adjacent small towns. Although these artificial community groupings are probably not the best obtainable, they correspond to fairly distinct community entities.

In the consideration of race and nationalities, only those communities were included wherein the majority of the selectees were of the same general nativity. Our findings are doubtless influenced to some extent by the fact that a minority of different mixed nationalities is represented in each community. One advantage of a community consideration, however, is the fact that persons of a given nationality in an immigrant community retain more of the characteristics and habits of that nationality than do those who have scattered as a minority into American communities. The data concerning the Irish, Italian, Portuguese, Jews and Old Americans are derived from a community consideration. Those concerning the Negroes and Chinese are based on a consideration of Negro and Chinese selectees, irrespective of community groupings here, since none of the groupings represented are predominantly Chinese or Negro.

The population density and socioeconomic level of each community were estimated. In preceding

in selectees from the communities of different predominant nationalities. The average density and socioeconomic level of each group of communities of similar nationality are also noted so that corrections can be made for differences that may be traceable to these causes. Socioeconomic ratings vary from A (best) to F (poorest). The most outstanding figures are the exceptionally high rate of disorders among the Negroes and Chinese. This is especially noteworthy in view of the fact that the figures for these two groups are based on individuals and therefore are not distorted by minorities of other nationalities. The table also shows that there is an obvious parallelism between the total mental disorders and the population density and socioeconomic level of each community represented. This parallelism is so marked that the table cannot be considered to present a clear picture of racial or national differences as such. The significance of racial and national differences becomes evident only when one considers the distribution of different mental disorders within each national grouping.

The Irish communities show high rates of psychopathic personality and chronic alcoholism (Table 2). These communities are high in density — from 10,000 to 20,000 per square mile — and are of the lowest (E and F) desirability. This fact may account for their high rate of psychopathy. The rate for chronic alcoholism cannot be similarly explained, since the Chinese, who live in a community that is at least as dense and as undesirable economically as those of the Irish, show an absence of alcoholism. Studies of hospital admissions have confirmed the findings that the rate of alcoholism

treatment with penicillin obscures the detection of a chancre in its early stages.

There were 2 patients in this series who, although they had received 60,000 units of penicillin, had been suspected of having a chancre. One case was diagnosed by dark-field examination, but in the other it was necessary to wait for the blood to become serologically positive. In the latter, a dorsal slit showed a scarred area on the corona that was apparently a healed lesion.

There were apparently only 2 patients in this series who had previously had gonorrhea. This is misleading, owing to the fact that once men are returned to duty, they may be hospitalized in any part of the world, making a thorough follow-up impossible.

SUMMARY

Two hundred cases of sulfonamide-resistant gonorrhea treated with penicillin have been reviewed and the findings and results tabulated. There were no toxic reactions, and all the patients were able to return to duty.

Penicillin has definitely proved its worth in the treatment of such cases. It has made it possible

to return these patients to duty in one third of the time previously required.

REFERENCES

1. Fleming, A. On antibacterial action of cultures of penicillin, with special reference to their use in isolation of *B. influenzae*. *Brit. J. Exper. Path.* 10:226-236, 1929.
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STUDIES IN MEDICAL SOCIOLOGY

III. The Relation of Mental Disorders to Race and Nationality

MAJOR ROBERT W. HYDE, M.C., A.U.S., AND STAFF SERGEANT RODERICK M. CHISHOLM, A.U.S.

BOSTON

RACIAL and national differences in admission rates to mental hospitals have been frequently studied, but there has never been an extensive study of such differences in the rate of mental disorders found in the population at large. The examination of selectees for induction into the armed forces provides a clear picture of the mental disorders in a cross section of the population, since selectees present the most unselected male group obtainable. The present study, based on data derived from the psychiatric examinations at the Boston Armed Forces Induction Station, shows the variation in rates for the major psychiatric disorders in communities grouped according to predominant nationality. An attempt is made to explain on a cultural basis those disorders that appear clearly to be connected with the predominant races or nationalities studied.

METHODS OF STUDY

Selectees from the eastern segment of Massachusetts within thirty-five miles of the coastline were examined at the Boston Armed Forces Induction Station. The period covered was the winter, spring and summer months of 1941 and 1942,

wherein 60,000 consecutive selectees were examined. A great diversity of population density is represented, at its greatest in Boston and least in the areas of Cape Cod and the farming areas to the north and south of Boston. Most of the area studied is highly industrialized, with a diversity of mills and factories, but significant sectors are devoted to farming and fishing. The age range of the selectees was from eighteen to forty-four, with most of them between twenty-one and thirty-eight. All social strata were represented, and the group may be said to form a representative cross section of the male population at large.

The people of the area represented a wide variety of nationalities. A few communities were of almost pure English stock, now in the sixth and seventh generation in this country; others, particularly in the dense areas, were of almost completely foreign parentage. The first extensive immigration after colonial times was that of the Irish in the middle of the nineteenth century. Since that time numerous Italians have moved into the commercial areas of Boston and other coastal towns. The Portuguese have moved into the fishing villages of Cape Cod and into Fall

and population density. It is not known whether the Negroes are forced to live at a level lower than that of the other population of the same community. The exceptionally high rate of mental disorders among them cannot be explained merely on the basis of population density or socioeconomic level. The Negroes show the highest rate for

TABLE 7. *Mental Disorders Among Negroes.*

DIAGNOSIS	REJECTION RATE %
Psychopathic personality	16.3
Mental deficiency	11.7
Psychoneurosis	6.7
Chronic alcoholism	2.2
Psychoses	0.3

psychopathy and psychoneurosis and, next to the Negroes, the highest rate for mental deficiency (Table 7).

The Old Americans are subject to fewer stresses than are any of the other groups here considered. Their pattern of disorders (Table 8) appears to be

TABLE 8. *Mental Disorders in Old American Communities.*

DIAGNOSIS	REJECTION RATE %
Psychoneurosis	2.7
Psychopathic personality	1.5
Mental deficiency	0.7
Chronic alcoholism	0.4
Psychoses	0.4

equally explained on the basis of the high socioeconomic level and intermediate population density of their communities.

DISCUSSION

Tables 1 through 8 indicate in general that, though density and economic level may be of major importance in the etiology of mental disorders, there are significant variations that can be explained only by reference to factors related to race or nationality. We shall attempt to show which differences are directly related to differences in density and economic level and which require reference to racial or national factors. In suggesting a cultural explanation of these variations, no attempt is made to minimize the importance of biology and heredity. Heredity and environment are so entwined that it is extremely difficult to weigh their relative importance. A community study of this sort, however, presents an excellent opportunity to note the significance of environmental factors. So little is known at the present time about the etiology of mental disorders that the best one can attempt to do is to suggest the ones that an adequate explanation ought to take.

It is assumed that the so-called "functional" mental disorders are manifestations of the emo-

tional stress and tension that result when the individual has been subjected to abnormal deprivations and frustrations. The most primitive outlets to stress are those of aggressiveness, belligerency, acquisitiveness, sexual freedom and other asocial conduct falling under the term "psychopathic personality." Chronic alcoholism is another primitive outlet, which may either be associated with aggressiveness or act as a substitute for it. When this type of outlet is blocked, the stress may manifest itself in another form. With cultural taboos against asocial conduct or alcoholism, stress may turn itself inward and the subject may then become psychoneurotic. Mental disorders thus depend partly on the acceptability of the outlet for stress.

Mental disorders also seem to depend upon the type of stress to which the individual is subjected. Aggressiveness follows on the frustration of elementary physical needs, but usually not frustration of more developed or "intellectual" needs. In the lowest economic level, where these higher-type needs have not had the opportunity to develop, the natural and accepted outlet to stress is psychopathy. In the more desirable communities where it is mainly the higher-type desires that are frustrated, the natural outlet is psychoneurosis. Indeed, as a rule it is only in the communities at the lowest point on the desirability scale, the F communities, that psychopathy prevails; one need only move up one step, to the E communities, to note a marked change in the pattern of mental disorders.

In addition to the frustrations and deprivations that are related directly to high population density and low socioeconomic level, there are further sources of stress to which most of the racial groups here considered are subject. When people are transplanted into a new and unfriendly environment, requiring different cultural standards and patterns of conduct, they are subject to varying difficulties of adaptation. Social and racial prejudice leads to inequality in the opportunities for jobs and housing, and suspicion and insults suffered at the hands of the dominant native population breed feelings of inferiority and resentment. When the prejudice is intense enough, the immigrants withdraw into segregated and isolated groups. Parents attempt to bring up their children according to the precepts of their Old World culture, at the same time that the children are attending American schools, speaking English and becoming Americans in appearance, habits and customs. The children are expected to adjust themselves to divergent cultures, and the resultant conflict tends to create both humiliation and disrespect for authority.

Numerous studies have shown that crime and delinquency rates are higher among the second generation than among the immigrant parents.⁷⁻⁹ Levy¹⁰ has attributed this to the conflict between

among the Irish is probably higher than those among other national groups for whom statistics are available.⁴ During World War I, the Irish

TABLE 2. *Mental Disorders in Irish Communities*

DIAGNOSIS	REJECTION
	RATE
	%
Psychopathic personality	5.9
Chronic alcoholism	3.0
Psychoneurosis	2.5
Mental deficiency	1.2
Psychoses	0.3

showed a significantly high rejection rate for so-called "alcoholic psychoses."⁵

Four Italian communities are represented. One of them is low in density, having from 1000 to 2000 persons per square mile, 1 is intermediate, and 2 are high, being over 20,000. The two densest communities are also of the lowest socioeconomic level (F). The least dense of the 4 communities has a desirability rating between D and E, and the other community has a C rating. The most noteworthy features of the Italian pattern are the high rate of mental deficiency and, as compared with the Irish, the relatively low rate of chronic alcoholism (Table 3). There is also a significant difference

TABLE 3. *Mental Disorders in Italian Communities*

DIAGNOSIS	REJECTION
	RATE
	%
Psychopathic personality	4.5
Mental deficiency	3.9
Psychoneurosis	3.8
Chronic alcoholism	1.2
Psychoses	0.4

between the Italians and the Irish in the incidence of psychopathy and psychoneurosis.

Four Portuguese communities are represented. Two are low in density (from 2000 to 5000), 1 is intermediate (from 5000 to 10,000), and 1 is moderately high (from 10,000 to 20,000). They range in desirability from C to E, inclusive. In contrast to the Italian pattern, psychoneurosis is the primary cause of psychiatric rejection and psychopathy is less important (Table 4). The Portuguese rate of mental deficiency is comparable to that of

TABLE 4. *Mental Disorders in Portuguese Communities*

DIAGNOSIS	REJECTION
	RATE
	%
Psychoneurosis	4.1
Mental deficiency	3.1
Psychopathic personality	2.4
Chronic alcoholism	0.6
Psychoses	0.1

the Italians. The incidence of mental deficiency among the Portuguese and Italians cannot be ex-

plained wholly in terms of economic level or population density.

There are three Jewish communities, 1 in the highest density (over 20,000) and 2 intermediate (from 10,000 to 20,000); 1 is at desirability level D 1 between D and E and 1 at E. The most interesting findings are the high rate of psychoneurosis and the low rate of alcoholism (Table 5). In United States draft statistics for the last war, the Jews were highest in psychoneurosis and among the lowest in "alcoholic psychosis,"⁵ and peacetime hospital

TABLE 5. *Mental Disorders in Jewish Communities*

DIAGNOSIS	REJECTION
	RATE
	%
Psychoneurosis	5.2
Psychopathic personality	2.6
Mental deficiency	1.0
Psychoses	0.4
Chronic alcoholism	0.2

statistics confirm these findings.⁶ Population density and socioeconomic level do not provide a satisfactory explanation of this pattern of mental disorders.

Boston's Chinatown is at the lowest desirability level and has a population density of over 20,000 per square mile. Although some of the Chinese registrants live elsewhere, the majority considered do live in Chinatown. The most interesting findings in Table 6 are the disproportionately high rate of mental deficiency, the low rate of psychopathy and the absence of alcoholism. This pattern, which

TABLE 6. *Mental Disorders Among Chinese*

DIAGNOSIS	REJECTION
	RATE
	%
Mental deficiency	24.5
Psychoneurosis	5.9
Psychopathic personality	1.2
Chronic alcoholism	0.0
Psychoses	0.0

cannot be explained on the basis of community desirability or population density, provides striking evidence of the significance of racial or national factors.

The term "mental deficiency" as applied to the Chinese is somewhat unfortunate, since the majority of the Chinese who are called mentally deficient are probably not feeble-minded in the ordinary usage of the term, but, as will be explained, are under so severe a cultural handicap that they are judged unable to absorb military training.

No single community represented among Selective Service boards is predominantly Negro. Although most of the Negroes live in dense communities of the lowest socioeconomic level, it is impossible to make proper corrections for socioeconomic

essions of immigrant stress; they suffer from adjustment resulting from a rural-urban shift, larger numbers come from rural areas in China; are deprived of many outlets by the presence of their families in China and by the shortage of Chinese women here. Yet the rate for psychopathy among them is comparatively low. This finding tends to indicate clearly the significance of racial factors in the etiology of mental disorders. Whether, in this case, the factors are biologic we cannot say, but it is clear that the culture of the Chinese has hindered both psychopathy and alcoholism unacceptable as outlets to stress. This rejection of violence is evident in the Chinese religious philosophy, which, like the religion of the Jews, serves to instill a deep respect for the law of the country. Psychoneurosis remains as the primary outlet for stress of the Chinese. Had those rejected for mental deficiency been able to express themselves more fully, psychoneurosis would probably have been used even oftener. (This error is not involved in the psychopathic or alcoholic groups, for adequate social-service records are available.)

The Negroes have the highest rate for both psychoneurosis and psychopathy. One reason for this may be that the Negroes in this study come from communities of varying densities and economic levels. A further and possibly more significant factor is the intensity and severity of the stress to which many of the Negroes are subjected. Aggressiveness is a natural reaction to physical stress, and when the stress is severe enough the individual is so completely oppressed that any impulse to aggressiveness is itself frustrated. When this happens the individual seldom hopes to overcome oppression and resigns himself to his distress. When he is thus discouraged, the principal outlet for his stress is psychoneurosis. It is probable that many of the Negro psychoneurotics fall into this group.

There is some correlation between the rates of chronic alcoholism (Table 10) and of psychopathy.

TABLE 10. Differences in Rejection Rates for Chronic Alcoholism in Communities of Different Predominant Nationalities.

NATIONALITY	REJECTION RATE
	%
Irish.....	3.0
Negroes.....	2.2*
Italian.....	1.2
Portuguese.....	0.6
Old American.....	0.4
Jewish.....	0.2
Chinese.....	0.0*

*Not community but individual figures.

In both cases, for instance, the Irish, Negroes and Italians, in varying order, are found to be the top three. But the rate for alcoholism among the Irish surpasses that of any other group. This variation cannot be explained in terms of socioeconomic level or

population density, for the Chinese, whose community is at least as dense and undesirable as those of the Irish, show an absence of alcoholism. Moreover, there is a marked difference between the Irish and the Italian communities in the rate for alcoholism, although there are no corresponding differences in density and desirability.

Alcohol among the Italians, Portuguese and Chinese is used primarily in the form of wine at mealtime and on festive occasions. It is seldom used in order to drown sorrow or to escape from physical and mental stress. Although wine may occasionally be taken to excess, the wine-drinking people have never been reported to have as much alcoholism as the hard liquor drinking nations of the north.

The Jews and the Chinese are lowest in the rate of alcoholism. The religion and culture of the Jews have restrained them from the social disgrace of drunkenness. The Chinese have not used alcohol as an emotional outlet, because to be drunk or disorderly brings shame on themselves and their families. (No Chinaman has yet been rejected for chronic alcoholism at this station.)

The high rate of alcoholism among the Negroes can be explained on the same basis as the high rate of psychopathy and psychoneurosis. The Negro is severely oppressed by all the types of stress mentioned; his impulse to aggressiveness is often in itself frustrated, and the result is that he is likely to become discouraged and broken. Alcoholism is an obvious outlet for this sort of stress, when alcohol is available.

The high rate of alcoholism among the Irish is less easily explained. It is known that alcohol has long been used freely by the Irish as a means of creating social conviviality after physical and nervous fatigue, and as a medicine, and its use in these ways has long been culturally acceptable. No other nationality in this study, with the possible exception of the Old American, uses alcohol in a manner similar to the Irish. The Old Americans, who are in a relatively secure social position, are subject to little or no abnormal stress and consequently are not in need of alcohol as an emotional outlet. We cannot determine to what extent alcohol would be used among the Old Americans were they under the same stress as the other groups. The Irish are subjected to a sufficient stress to permit an easy extension of their normal use of alcohol.

The rate of mental deficiency among the Chinese, Negroes, Italians and Portuguese (Table 11) is disproportionately high. Our figures are misleading, however, unless they are interpreted in terms of a number of racial and cultural factors.

Probably some of these findings can be attributed to the unavoidable limitations of our psychometric examination. We know that some members of these groups have resented being drafted and

the demands of the parents and the demands of society. Klineberg¹¹ remarks that the very fact that criminality "appears in the second and not in the first generation makes it clear that it cannot have a racial or biological basis, since this is obviously the same for both groups."

Large numbers of Italians, Negroes, Portuguese and Chinese have migrated from rural to urban communities. In rural communities there is little organized control of the individual's conduct other than that enforced by the social pressure of the group. The influence of law is unimportant, weak or resented. There is more respect for common labor, fewer broad class barriers based on material wealth, greater physical security and less concern for luxuries. These values are changed with movement into urban society. Because of the extent of adaptation necessary in the changing to a greatly divergent cultural pattern, this rural-urban shift usually brings cultural disorganization, with attendant increase in crime, delinquency, alcoholism, ambition and selfishness.

These stresses provide a plausible explanation of some of our findings. This is evident in racial and national variations in psychopathy and psychoneurosis, in the marked differences in the incidence of chronic alcoholism and in the disproportionately high rate of mental deficiency in some national groups. Sufficient data on the psychoses to warrant any generalization are not available.

The high incidence of psychopathy among the Negroes, Irish and Italians (Table 9) is easily explained. Each of these groups is subject to the stresses that accompany population density and low socioeconomic level. They are immigrant groups and, in varying degrees, have met with suspicion and hostility on the part of the Old Americans. Large numbers of them have undergone the disorganization involved in a rural-urban shift. The Italians, and particularly their children, — the

frustrations and deprivations mentioned above, as well as by many others. Psychopathy is the natural reaction to such stress, and it is acceptable in the undesirable communities from which most of the people come.

Since the Irish and the Italians have a culturally acceptable outlet in psychopathy, the rate of psychoneurosis is correspondingly low. It is lower among the Irish, possibly because they find a further outlet in alcoholism. Psychoneurosis is the primary cause of psychiatric rejection among the Portuguese, whereas psychopathy is the primary cause among the Irish and Italians. This probably can be explained in terms of socioeconomic level. The Irish and the Italians live in the most undesirable communities, and most of the Portuguese live in E and D communities. Although the E and D communities are low in desirability scale, it has been found that extreme psychopathy is to be expected only at the very lowest level, that is, in the truly slum areas.² Once one starts to move up the socioeconomic ladder, psychopathy becomes increasingly inhibited.

The low incidence of psychopathy, coupled with the high rate of psychoneurosis, among the Jews is not difficult to account for. The Jews seem to have acquired a special aptitude for adaptation to a new environment after centuries of migration into unfriendly surroundings. They have even devised special aids, such as the Hebrew Immigrant Aid Society, to smooth the early steps of adaptation for the immigrant, preventing his settling in the worst slums. The desirability level of their communities is higher than those of the Irish, Italians and Negroes. The stresses to which Jews are subjected in this area are not primarily those of frustration of their elementary physical needs, and consequently not such as to arouse psychopathy as a natural reaction. Further, their culture has been one dominated by a strong religion, which restrains them from asocial conduct. For centuries they have offered no military resistance to oppression. "I adjure you that if the government decrees harsh decrees, rebel not against any matter that it imposes upon you" (Ecclesiastes viii, 2). The asocial conduct of the psychopath has become culturally taboo and, as will be noted, the Jew is restrained from alcoholism. Accordingly, the principal outlet for his stress is psychoneurosis. Myerson⁶ attributes to the Jew "an apprehensiveness and an emotionality that arose from the conditions of life to which his Christian neighbors subjected him."

One of the interesting findings indicated in Table 9 is the comparatively low rate of psychopathy among the Chinese. The majority of the Chinese considered are subject to at least the same sources of stress as are the Irish and the Italians. They live in one of the densest and most undesirable communities, and are burdened by all the

TABLE 9. Differences in Rejection Rates for Psychopathic Personality and Psychoneurosis in Communities of Different Predominant Nationalities.

PSYCHOPATHIC PERSONALITY		PSYCHONEUROSIS	
NATIONALITY	REJECTION RATE	NATIONALITY	REJECTION RATE
	%		%
Negro	16.3*	Negro	6.7*
Irish	5.9	Chinese	5.9*
Italian	4.5	Jewish	5.2
Jewish	2.6	Portuguese ..	4.1
Portuguese ..	2.4	Italian	3.8
Old American ..	1.5	Old American ..	2.7
Chinese	1.2*	Irish	2.5

*Not community but individual figures.

generation now being examined for induction, — have been submitted to a conflict between American society and the culture of their parents. The Negroes have been severely oppressed by all the

pressions of immigrant stress; they suffer from adjustment resulting from a rural-urban shift, larger numbers come from rural areas in China; they are deprived of many outlets by the presence of their families in China and by the shortage of Chinese women here. Yet the rate for psychopathy among them is comparatively low. This finding tends to indicate clearly the significance of racial factors in the etiology of mental disorders. Whether, in this case, the factors are biologic we cannot say, but it is clear that the culture of the Chinese has hindered both psychopathy and alcoholism unacceptable as outlets to stress. This rejection of violence is evident in the Chinese religious philosophy, which, like the religion of the Jews, serves to instill a deep respect for the law of the country. Psychoneurosis remains as the primary outlet for stress of the Chinese. Had those rejected for mental deficiency been able to express themselves more fully, psychoneurosis would probably have been found even oftener. (This error is not involved in the psychopathic or alcoholic groups, for adequate social-service records are available.)

The Negroes have the highest rate for both psychoneurosis and psychopathy. One reason for this may be that the Negroes in this study come from communities of varying densities and economic levels. A further and possibly more significant factor is the intensity and severity of the stress to which many of the Negroes are subjected. Aggressiveness is a natural reaction to physical stress, but when the stress is severe enough the individual is so completely oppressed that any impulse to aggressiveness is itself frustrated. When this happens the individual seldom hopes to overcome oppression and resigns himself to his distress. When he is thus discouraged, the principal outlet for his stress is psychoneurosis. It is probable that many of the Negro psychoneurotics fall into this group.

There is some correlation between the rates of chronic alcoholism (Table 10) and of psychopathy.

TABLE 10. Differences in Rejection Rates for Chronic Alcoholism in Communities of Different Predominant Nationalities.

NATIONALITY	REJECTION RATE
	%
Irish.....	3.0
Negroes.....	2.2*
Italian.....	1.2
Portuguese.....	0.6
Old American.....	0.4
Jewish.....	0.2
Chinese.....	0.0*

*Not community but individual figures.

In both cases, for instance, the Irish, Negroes and Italians, in varying order, are found to be the top three. But the rate for alcoholism among the Irish surpasses that of any other group. This variation cannot be explained in terms of socioeconomic level or

population density, for the Chinese, whose community is at least as dense and undesirable as those of the Irish, show an absence of alcoholism. Moreover, there is a marked difference between the Irish and the Italian communities in the rate for alcoholism, although there are no corresponding differences in density and desirability.

Alcohol among the Italians, Portuguese and Chinese is used primarily in the form of wine at mealtime and on festive occasions. It is seldom used in order to drown sorrow or to escape from physical and mental stress. Although wine may occasionally be taken to excess, the wine-drinking people have never been reported to have as much alcoholism as the hard liquor drinking nations of the north.

The Jews and the Chinese are lowest in the rate of alcoholism. The religion and culture of the Jews have restrained them from the social disgrace of drunkenness. The Chinese have not used alcohol as an emotional outlet, because to be drunk or disorderly brings shame on themselves and their families. (No Chinaman has yet been rejected for chronic alcoholism at this station.)

The high rate of alcoholism among the Negroes can be explained on the same basis as the high rate of psychopathy and psychoneurosis. The Negro is severely oppressed by all the types of stress mentioned; his impulse to aggressiveness is often in itself frustrated, and the result is that he is likely to become discouraged and broken. Alcoholism is an obvious outlet for this sort of stress, when alcohol is available.

The high rate of alcoholism among the Irish is less easily explained. It is known that alcohol has long been used freely by the Irish as a means of creating social conviviality after physical and nervous fatigue, and as a medicine, and its use in these ways has long been culturally acceptable. No other nationality in this study, with the possible exception of the Old American, uses alcohol in a manner similar to the Irish. The Old Americans, who are in a relatively secure social position, are subject to little or no abnormal stress and consequently are not in need of alcohol as an emotional outlet. We cannot determine to what extent alcohol would be used among the Old Americans were they under the same stress as the other groups. The Irish are subjected to a sufficient stress to permit an easy extension of their normal use of alcohol.

The rate of mental deficiency among the Chinese, Negroes, Italians and Portuguese (Table 11) is disproportionately high. Our figures are misleading, however, unless they are interpreted in terms of a number of racial and cultural factors.

Probably some of these findings can be attributed to the unavoidable limitations of our psychometric examination. We know that some members of these groups have resented being drafted and

as a result were not motivated to their best performance. Every practicable precaution against malingering is taken, but low motivation is important in borderline cases, and it is probable that

TABLE 11. *Differences in Rejection Rates for Mental Deficiency Found in Communities of Different Nationalities.*

* PREDOMINANT NATIONALITY	REJECTION RATE
	%
Chinese	24.5*
Negro	11.7*
Italian	3.9
Portuguese	3.1
Irish	1.2
Jewish	0.9
Old American	0.7

*Not community but individual figures.

many who were rejected might have been accepted as borderline had they been better motivated. Further, although our psychologic tests are designed to measure intelligence or ability to learn, as distinguished from education or information, we cannot claim that this intention is realized in every case. The Chinese and, to a lesser extent, the Negroes and Portuguese seem to have insufficient familiarity with the materials from which some of the tests have been constructed, and this lack of familiarity may often result in an invalid performance.

Possibly the best cultural explanation of these findings is provided by the theory that apparent mental deficiency, in many cases, is merely a reaction to emotional stress. Dollard,¹² in his study of caste and class in southern towns, noted that the frustrated Negro, unable to find any aggressive outlet for his stress, unconsciously assumed an attitude of stupidity. In this way the completely discouraged individual was enabled both to incur revenge and to exempt himself from disagreeable responsibilities. Maslow and Mittelman¹³ insist that this apparent stupidity is an unconscious mechanism. They state: "This roundabout and inefficient path is chosen because the individual's fundamental needs have in one fashion or another been frustrated or come into conflict with one another. Give him back his self-esteem and his feeling of security, and his symptoms—whether apparent stupidity or hostility or compulsion—tend to disappear." The Laotian philosophy, as Lin Yutang has reminded us, has taught the Chinese that there is wisdom in "embracing folly."

Our figures concerning the Chinese are not strictly comparable with those of the other groups. It is not true that 24.5 per cent of the Chinese are feeble-minded. What this figure means is that this percentage of the Chinese were judged, in view of their apparently complete inability to understand

English, to have insufficient endowment to absorb Army training in the time provided for such purposes.

The low rate of mental deficiency among the Jews is not difficult to explain. Their stress is such as to provoke psychoneurosis. Unlike the Negroes, they are not so severely oppressed that they must resort to apparent stupidity as an exemption. Education has always been venerated by the Jews, since it has been necessary in their preservation under oppression ("Mine anointed are the school children. My prophets are the scholars."—*Chron.* xvi, 22). Their low rate on failure of mental tests can be attributed partly to their higher education, to the cultural opportunities afforded by their urban background and to their intense motivation to make high scores.

SUMMARY

At the Boston Armed Forces Induction Station the rejection rates for five types of mental disorders among seven different national or racial groups were determined.

The Negroes, Irish and Italians have high rates for psychopathic personality and chronic alcoholism; the Negroes, Chinese, Russian Jews and Portuguese for psychoneurosis; and the Chinese, Negroes, Italians and Portuguese for mental deficiency. The Negroes have high rates for all five types of disorder. The Old Americans have comparatively low rates.

These findings are partly explained in terms of the socioeconomic level, population density and the cultural differences of the different nationalities.

This study presents sufficient evidence of cultural differences as etiologic factors in mental disorders to suggest both the need of further investigation in this direction and the possibility of extensive application of mental hygiene.

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PHYSICAL THERAPY IN WARTIME*

K. G. HANSSON, M.D.†

NEW YORK CITY

IN WARTIME most human endeavors are accelerated. This applies especially to medicine, and all the specialties are included. This paper attempts to discuss how physical therapy has come to war," and also points out lessons from the war that will undoubtedly influence civilian hospitals in the future. It is a pleasure to testify that it was Dr. Brackett and Dr. Goldthwait, of Boston, who were mainly responsible for the establishment of physical therapy in World War I, and that it was Dr. Granger, of Boston, who represented physical therapy in the Surgeon General's office during the last war.

During the present war, the Surgeon General is ordered that general and other large hospitals in the continental United States be provided with standard equipment for electrotherapy, hydrotherapy and thermotherapy, with gymnasium apparatus and with equipment for research. Most of the American hospitals in Alaska, Australia, Africa and Italy and at other operational bases are similarly equipped. These departments of physical therapy are under the direct supervision of one or more medical officers trained in this field. The aides must have the same training as that required by the American Medical Association, and were commissioned by an act of Congress in February, 1943. The Army has also assigned certain hospitals for specific treatment, such as the Walter Reed General Hospital for amputation cases, the Ashford General Hospital for arthritis, and the Fitzsimons General Hospital for rehabilitation.

The amount of work done in a physical-therapy department may be judged from the July, 1943, report from the Lawson General Hospital, where 10,056 treatments were given. The types of cases treated do not differ much from those in civilian life. They are back injuries, painful feet, knee injuries, strains, sprains, dislocations, fractures and burns. Now, however, since combat casualties are arriving, there is an increase in fractures, nerve injuries, burns and wounds of the soft tissue. The treatment of these cases is much the same as that in civilian hospitals, with special emphasis on whirlpool baths, occupational therapy, active exercises and massage.

Physical therapy in the Navy is similar to that in the Army, but owing to ship regulations much

of the work is done by more or less trained corpsmen or pharmacists' mates.

* * *

One of the outstanding contributions of the war so far has been the revision of convalescent care; this may be called rehabilitation, reconditioning or streamlined convalescence. The fact is that the uses and abuses of bed rest are being analyzed. It is evident that the increased supply of hospital beds, the development of the profession of nursing and the widespread use of hypnotics and narcotics are largely responsible for the present use of absolute bed rest. It has become familiar to all to see wards full of patients lying flat in bed, absolutely quiet and guarded against moving by nurses. The solid foundations of bed rest as a therapeutic measure, however, are being shaken, and absolute rest is being challenged. The facts that it costs \$20,000 to train a pilot and that it is more economical to cure such a patient than to train a new pilot may be the original cause of this revision of convalescence. It seems rational to review some of the factors concerning bed rest, and to describe certain of the physical-therapy measures to be used to discharge a patient in a better general condition than that when he entered the hospital. By discussing the various body systems separately, it may be possible to draw some conclusions concerning rest *versus* activity.

Skeleton. The posture that a patient assumes in bed is physiologically abnormal. A painful neck, an aching back and stiff knees are frequent symptoms of bed rest. Their occurrence can be prevented by the knowledge and application of proper body mechanics. Immobilization produces a negative calcium balance, which in turn may be counteracted by proper ultraviolet radiation every other day, either individually or, as is done at the New York Hospital, in specially built solariums equipped with powerful Finsen carbon arcs. Stiffness of the joints can be prevented by active or passive exercises at prescribed intervals.

Muscular system. The muscles are intended for activity, and when they are deprived of this, they become stiff, lose their tone and may go on to atrophy. Massage eliminates the lactic acid and carbon dioxide responsible for the stiffness, and muscle-setting exercises maintain tone and prevent atrophy.

Circulatory system. The circulatory system is probably the greatest sufferer from complete bed rest. Hyperemia, congestion and edema are frequent. It is less generally realized that constant

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

†Assistant professor of clinical surgery, Cornell University Medical College, director of physical therapy, Hospital for Special Surgery and New York Hospital.

pressure on the veins in the calves may cause thrombosis, which in turn may be responsible for pulmonary emboli. Autopsies show that 30 per cent of all hospital patients have thrombi in the veins of the calves. In adults who have been in bed two weeks or longer, the incidence reaches 60 per cent. All show necrosis and inflammatory reactions in the calf muscles, which apparently initiate the process. Of the last 300 adult patients autopsied at the New York Hospital, 5 per cent died of pulmonary embolisms secondary to thrombi in the legs. This equals the number of deaths from cancer of the stomach, and the fatalities are considered due to complete bed rest. Such serious circulatory disturbance can be prevented by systematized exercises and changes of position in bed. This regime also maintains an adequate blood pressure and prevents dizziness when getting up.

Gastrointestinal system. The constipation of the bedridden patient is usually accepted as unavoidable, and many people ascribe their chronic constipation to previous confinement in bed. The objectionable bedpan is probably a contributory agent. The straining on a bedpan is probably underestimated, the danger of bathroom privileges is overestimated, and the result is that the patient becomes constipated from bed rest. It has been shown that there is no significant difference in the loss of energy from sitting as against that from lying flat in bed. In the Scandinavian countries abdominal massage is much in vogue to counteract constipation. If more abdominal massage were used, permission for sitting up and bathroom privileges were granted oftener and bedpans were less used, constipation from bed rest could be managed better than with the cathartic pill of some patent medicine.

Skin. Irritation of the skin is obvious and receives the immediate attention of the nurse. It has increased in frequency owing to the chemicals used in modern hospital laundries. Skin ulcers and bedsores are often considered the result of poor nursing, but bed rest is equally responsible. It is questionable whether the daily alcohol rub is the best solution, and whether it would not be physiologically sounder to use some fatty-acid application, together with changes in positions, and ultraviolet radiation.

Nervous system. Regarding the nervous system, the mind suffers most from being confined to one room and immobilized in bed. The rules of hospitalization regulate patients' days and nights so that they have no more responsibilities and have much time to feel sorry for themselves. At night, when darkness shuts out most external impressions,

painful sensations are increased. Occupational therapy is available to counteract many of the mental reactions of bed rest, and functional occupational therapy is most important to regain action.

* * *

In my visits to various reconditioning centers I have been impressed by this new conception of convalescence, but on closer inspection one finds that the medical officers are handicapped by a lack of trained personnel to carry out these ideas. The actual work of the convalescent program is usually carried out by men trained in physical education. They are all eager and enthusiastic, but the realization of these new rational ideas is not without danger. Great discrimination must be used in selecting the patients and the type of exercises to be employed. One gains the impression that the medical departments of the armed services have contributed a valuable advance in medical care, and it is to be hoped that this contribution can be put on a rational basis. Physical therapy has a very important part to play in this convalescent program. It is needless to point out that no radical departure from the rest treatment in tuberculosis, hypertension or comparable patients is advocated but this revision of the traditional hospitalization of patients must be considered in civilian practice. The advantage of the so-called "Kenny treatment" of poliomyelitis is not that it cures more patients than other methods but that the early application of activities turns out patients in better general health and with better circulation and muscular function than the old immobilization treatment produced.

Physical therapy has many contributions to offer when one considers the immediate necessity for shortening hospitalization, not only in the armed services but also in civilian life. It is high time to bring physical therapy into the wards of civilian hospitals. There has been a tendency to centralize it in a department. This is still necessary in many applications, such as hydrotherapy, mechanotherapy, underwater exercises, electrotherapy and so forth, but the time has come to attempt more active treatment of the bedridden patient. Physical therapy can be utilized to shorten the stay in bed, to counteract many deplorable results of bed rest and to turn out a discharged patient with more adequate circulation, better muscular tone, better posture, a normally functioning gastrointestinal tract, better skin and a mind that is mentally alert instead of depressed.

321 East 42d Street

MEDICAL PROGRESS

PARENTERAL-FLUID THERAPY

The Estimation of Losses Incident to Starvation and Dehydration with Acidosis or Alkalosis and the Provision of Repair Therapy*

ALLAN M. BUTLER, M.D.,† AND NATHAN B. TALBOT, M.D.‡

BOSTON

THE first part of this review of parenteral-fluid therapy⁶⁷ the parenteral provision of the maintenance needs was considered. This deals with the parenteral repair of the losses of water and electrolyte incident to dehydration. For patient requiring parenteral therapy has suffered starvation and severe dehydration, the amount and type of the losses must be estimated, and appropriate repair needs must be provided parenterally in addition to the maintenance requirements.

CLINICAL APPRAISAL OF DEHYDRATION

The extent of the dehydration cannot be estimated reliably by any single laboratory procedure.⁵² Serial determinations of body weight, blood hemoglobin concentration,⁶⁸ red-cell and white-cell counts, plasma protein⁶⁹ and nonprotein nitrogen concentrations may contribute to a retrospective appraisal of the degree of the dehydration and the response to therapy, but even such serial determinations will not provide the pertinent information obtained by a careful history and physical examination and by the continued detailed clinical observation of the patient during therapy.

The history of weight loss, dietary and fluid intake and losses by urine, stool, vomiting, insensible sweating or other routes, together with the symptoms, indicate the nature and extent of the dehydration and fluid loss. In addition, they suggest probability of acidosis or alkalosis being associated with the dehydration.^{52, 70, 71}

By physical examination the clinical appraisal of the weight loss, tongue, mucous membranes, skin color, hydration of the eye and periocular tissue, heart action, peripheral circulation, fecal masses in the bowel, stools, urine volume and concentration. In the infant, the fontanelle further define the extent of the dehydration and starvation. Muscular hypertonicity, hyperactive reflexes, a positive Tostek or Trousseau sign or carpopedal spasm suggests alkalosis. Deep and exaggerated respirations confirm the probability of metabolic acidosis.⁷⁰⁻⁷⁴ or primary stimulation of the respiratory center with respiratory alkalosis.^{52, 70, 71, 73-76} In the case of extreme shock or emphysema, shallow irregular respirations support the probability of acidosis.^{52, 70, 71, 77, 78} Great caution must be taken

in using the urinary pH as an index of acidosis or alkalosis. Renal infection may render the urine alkaline in acidosis. In the dehydration of alkalosis the urine may be acid if the cation or sodium concentration of the plasma is below normal, as not infrequently occurs.^{70, 78}

Adequate nurse's notes detailing intake and output and signs and symptoms and frequent re-examination of the patient by the physician reveal much concerning the response to therapy.

In the early stages of appraisal and therapy, readily obtainable clinical information utilized with reasonable clinical judgment is far more valuable than the usually available laboratory determinations. Too often these latter in being substituted for clinical acumen provide little or misinterpreted information. For example, as discussed later and illustrated in Figure 1, a patient with an abnormally low plasma or blood carbon dioxide content may be suffering either from a metabolic acidosis — as in diarrhea or diabetic coma — or from a respiratory alkalosis — as in the hyperpnea of hysteria or encephalitis.^{52, 70, 71, 73-75, 77} As parenteral therapy proceeds, however, certain laboratory analyses, as discussed in the last section below, are guides essential to the provision of the best therapy.

Ordinarily, most of the weight loss during acute dehydration with starvation is due to loss of body water. Approximately half the loss comes from the extracellular fluids containing Na^+ , Cl^- and HCO_3^- , and half from the intracellular fluids containing K^+ , Mg^{++} , HPO_4^{--} , SO_4^{--} and protein.^{71, 79-84} A loss of between 8 and 12 per cent of the body weight represents significant dehydration. Hence the extracellular and intracellular losses may be estimated, as subsequently outlined in Table 1.

It is interesting that a relatively large intracellular fluid loss occurs following hemorrhage.⁸⁵

Rarely, when dehydration occurs at an extremely rapid rate with loss of the extracellular electrolytes Na^+ and Cl^- , — as occurs in a hot box or under anesthesia in a hot operating room or by loss of interstitial fluid while ingesting water, — the plasma volume may be reduced so rapidly that circulatory collapse occurs before marked generalized dehydration has an opportunity to develop.^{69, 80, 86}

EXTRACELLULAR LOSSES AND REPAIR

Qualitatively, the extracellular losses vary with the route of loss.^{70, 71, 87-89} For example, in vomiting

*From the Children's Medical Service, Massachusetts General Hospital, the Department of Pediatrics, Harvard Medical School.

†Chief of the Children's Medical Service, Massachusetts General Hospital, and associate professor of pediatrics, Harvard Medical School.

‡Assistant physician, Children's Medical Service, Massachusetts General Hospital, and associate in pediatrics, Harvard Medical School.

pressure on the veins in the calves may cause thrombosis, which in turn may be responsible for pulmonary emboli. Autopsies show that 30 per cent of all hospital patients have thrombi in the veins of the calves. In adults who have been in bed two weeks or longer, the incidence reaches 60 per cent. All show necrosis and inflammatory reactions in the calf muscles, which apparently initiate the process. Of the last 300 adult patients autopsied at the New York Hospital, 5 per cent died of pulmonary embolisms secondary to thrombi in the legs. This equals the number of deaths from cancer of the stomach, and the fatalities are considered due to complete bed rest. Such serious circulatory disturbance can be prevented by systematized exercises and changes of position in bed. This regime also maintains an adequate blood pressure and prevents dizziness when getting up.

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tion of sodium chloride higher or lower than the normal serum sodium and chloride concentrations of 322 and 365 mg. per 100 cc. respectively? Or, if a 0.85 per cent solution of sodium chloride is infused fairly rapidly into a dehydrated patient whose kidneys are not functioning adequately, as indicated by an elevated nonprotein nitrogen, will the serum Cl^- level tend to be elevated or lowered? And if the serum Cl^- level is lowered or elevated by 35 mg. per 100 cc., by how many volumes per cent will the carbon dioxide tend to be changed? Perhaps to answer this, one would need to know the effect of the infused saline on the serum Na^+ concentration. These, of course, are questions that everyone can answer readily, because one could hardly use physiologic saline solution parenterally without knowing the answers. But the answers are readily given because, instead of the difficultly integrated units of concentration used above, a single unit of chemical equivalents is generally used in expressing the concentrations of electrolytes in body fluids. The utilization of chemical equivalents as the unit of concentration is logical, because the demand of electroneutrality of the body fluids prescribes an equality or balance of the sum of the electropositive ions (cations) and the sum of the electronegative ions (anions). This unit therefore permits visualization and appraisal of the disturbances in the balance of cations (bases) and anions (acids) in which one is clinically interested. Custom and the order of magnitude of these concentrations in body fluids render the milliequivalent† per liter of solution or per liter of water a convenient and accepted unit of concentration in clinical medicine, as evidenced by all the references given in this review. In considering the equilibrium of electrolytes in the different compartments of body fluids, concentrations expressed as milliequivalents per liter of water are preferable, but the more easily determined milliequivalents per liter of solution suffice for considerations of parenteral fluid therapy.

The accepted normal plasma concentrations in milliequivalents per liter of plasma are as follows:

CATIONS		ANIONS	
Na	138	HCO_3^-	26
K	5	Cl	103
Ca	5	HPO_4^-	2
Mg	2	SO_4^-	1
		Organic acid	2
		Protein	16
Total	150	Total	150

*The custom of expressing plasma Cl concentrations as milligrams of sodium chloride per 100 cc. is, of course, illogical, since the Na and Cl concentrations of plasma are not equal.

The carbon dioxide dissolved as undissociated carbonic acid is normally 1.3 millimoles per liter. As the total carbon dioxide determined in the clinical laboratory is the sum of this dissolved carbon dioxide and the HCO_3^- , the normal total plasma

carbon dioxide equals 1.3 plus 26, or approximately 27 millimoles per liter.

Physiologic saline (0.85 per cent sodium chloride) solution contains 145 milliequiv. of Na^+ and 145 milliequiv. of Cl^- per liter.

Using the milliequivalent one can readily appreciate, as shown by the diagrams in Figures 1 and 2, that the Cl^- concentration of physiologic saline solution is appreciably higher than that of normal serum. Therefore, the infusion of such saline solution tends to elevate the serum Cl^- level. This of course tends to lower the HCO_3^- and thus the total carbon dioxide level, a rise of 10 milliequiv. Cl^- tending to effect a 10-milliequiv. lowering of the HCO_3^- . Since the normal HCO_3^- concentration is but 26 milliequiv. per liter, this is a significant reduction. Such an infusion of physiologic saline solution, however, has but little effect on the serum Na^+ concentration. Since the milliequivalent makes all this clear, it is odd that physicians have often resented rather than welcomed its use.

Gamble's⁹⁷ graphic presentation of the anatomy and vicissitudes of the extracellular fluids^{74, 98} profusely illustrates how the milliequivalent facilitates the clinical appraisal of a patient's status with respect to cation-anion equilibrium, — that is, acidosis and alkalosis, — and thus simplifies clinical thought concerning electrolyte and water metabolism.

Such graphic presentation of the composition of normal plasma and of the plasmas of patients suffering from the dehydration, starvation and metabolic alkalosis of gastric vomiting, from the respiratory acidosis of asthma, from the dehydration, starvation and metabolic acidosis of severe diarrhea and from the respiratory alkalosis of primary hyperventilation is presented in Figure 1. Figure 2 similarly presents the composition of physiologic saline solution, of 1/7 molar sodium bicarbonate solution

†An equivalent is the weight of an ion which, in neutralization reactions, is equivalent to 1 gram-atom of hydrogen. Thus, the number of milliequivalents per liter is equal to the milligrams per 100 cc. times ten divided by the equivalent weight, which, in turn, is the atomic weight divided by the valence. For example,

$$322 \text{ mg. sodium per } 100 \text{ cc.} = \frac{322 \times 10}{23} = 140 \text{ milliequiv. Na per liter.}$$

$$365 \text{ mg. chloride per } 100 \text{ cc.} = \frac{365 \times 10}{35.5} = 103 \text{ milliequiv. Cl per liter.}$$

$$10 \text{ mg. calcium per } 100 \text{ cc.} = \frac{10 \times 10}{20} = 5 \text{ milliequiv. Ca per liter.}$$

$$60 \text{ vol. per cent carbon dioxide} = \frac{60 \times 10}{22.4} = 27 \text{ millimoles carbon dioxide.}$$

per liter, where 22.4 equals the liters of carbon dioxide that at 0°C. and 1 atmosphere of pressure contain 1 mol of carbon dioxide. In normal plasma, in which the ratio of HCO_3^- to H_2CO_3 is 20:1, 27 mm. of carbon dioxide per liter is equal to 1.3 mols of carbonic acid plus 25.7 milliequiv. of HCO_3^- per liter. Therefore, the following approximation satisfies clinical purposes:

$$\frac{\text{Vol. per cent carbon dioxide}}{2.3} = \text{milliequivalents } \text{HCO}_3^- \text{ per liter.}$$

there is a greater loss of Cl^- than of Na^+ , with a resultant tendency to alkalosis.^{77, 90} The alkalosis organic and organic acid catabolites and a diminution in the renal excretion of cations (bases)

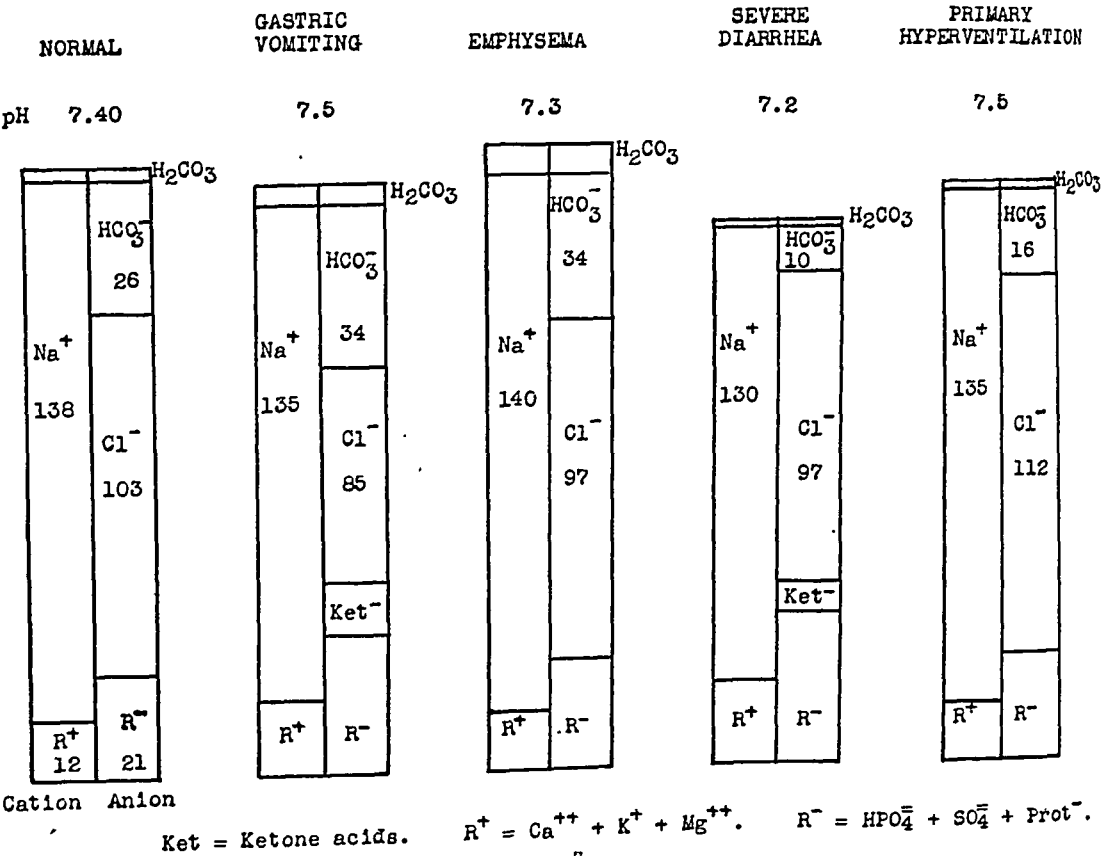


FIGURE 1. Diagrammatic Representation (according to Gamble) of the Electrolyte Composition of the Plasma of a Normal Subject, a Patient with the Metabolic Alkalosis of Gastric Vomiting, a Patient with the Respiratory Acidosis of Asthma, a Patient with the Metabolic Acidosis of Severe Diarrhea and a Patient with the Respiratory Alkalosis of Hysterical Hyperventilation.

The numerical values for Na, HCO₃ and Cl represent milliequivalents per liter. The sums of other cations and anions are given merely to show their relative order of magnitude and direction of change in concentration. Similarly the undissociated mols of carbonic acid are diagrammed roughly to indicate the direction of change. The reaction (pH) is proportional to the ratio of the HCO₃ to the carbonic acid.^{52, 70, 71}

is then partially compensated by the excretion of Na^+ and K^+ with HCO_3^- in an alkaline urine.⁹¹

TABLE 1. Calculations for Approximating the Extracellular Parenteral Needs, Over and Above the Maintenance Needs, of Dehydrated Acidotic Patients.

CONSIDERATION	5-KG. INFANT	60-KG. ADULT
Fluid loss:		
Weight before dehydration	5000 gm.	60000 gm.
Weight after dehydration	4400 gm	54000 gm.
Approximate total fluid loss	600 cc.	6000 cc.
Extracellular loss = half total loss . . .	300 cc.	3000 cc.
Intracellular loss = half total loss . . .	300 cc.	3000 cc.
Provision of repair needs:		
One part M/7 sodium bicarbonate* + two parts physiologic saline solution for extracellular loss and acidosis . .	300 cc.	3000 cc.
Serum for protein depletion†	100 cc.	800 cc.
Whole blood for hemoglobin and protein depletion‡	100 cc.	500 cc.

*Or M/7 sodium lactate.
†To be given if the serum protein level is low before or during parenteral therapy.
‡To be given if the red-cell count or hemoglobin level and serum protein level are low before or during parenteral therapy.

As the dehydration progresses the renal function is impaired,^{92, 93} with a resultant retention of in-

bicarbonates.^{70, 78} In diarrhea two factors dispose to acidosis. First, there is a greater in diarrheal stools of sodium and other cat (bases) than of chloride and other anions (acids). Second, the impaired renal function incident to dehydration results in the retention of acid ca olites.^{70, 71, 87, 88, 96} Starvation ketosis tends develop in both the alkalotic dehydration of vo ing and the acidotic dehydration of diarrhea.

Diagrammatic visualization of the disturba in the balance of cations (bases) and anions (ac greatly facilitates comprehension of the pathol physiology of the extracellular fluids.⁷¹ Utiliza of unrelated units of concentration, such as n grams per 100 cc. of chloride and volumes per of carbon dioxide for serum and grams of sod chloride per 100 cc. for physiologic saline s tion, makes such visualization impossible and ders thinking difficult. For example, are the l and Cl^- concentrations of a 0.85 per cent s

days when sterile sodium bicarbonate and sodium lactate solutions¹⁰⁴ were available, 10 per cent dextrose was added to the physiologic saline solution to so increase blood flow and improve renal function that the excess Cl^- could be excreted promptly.^{88, 95} The resulting increase in urine volume favored the urinary excretion of Cl^- , nonprotein nitrogen and other catabolites and the acidosis was ultimately corrected. Fortunately, sterile solutions of sodium bicarbonate or sodium lactate are readily available today. Therefore physiologic saline solution may be so diluted with these solutions that its hypertonicity in Cl^- is corrected and efficient hydration of the acidotic patient may be accomplished without delay in correcting the acidosis and hyperpnea. For example, the third diagram in Figure 2 depicts the concentrations obtained by diluting two parts of 0.85 per cent saline solution with one part of 1/7 molar sodium bicarbonate solution. Because this mixture has an HCO_3^- content almost double that of normal plasma, — that is, 48 milliequiv. per liter, — its infusion to a dehydrated acidotic patient with a low plasma HCO_3^- level and pH (fourth diagram Fig. 1) elevates the lowered plasma and extracellular bicarbonate and thus tends to correct the acidosis. At the same time, because the Na^+ and Cl^- concentrations of this mixture approximate those of normal plasma, it favors the restoration of normal serum Na^+ and Cl^- concentrations while repairing the deficit of extracellular electrolytes. One-seventh molar sodium lactate solution may usually be substituted for the NaHCO_3 solution, since the lactate ion appears to be oxidized to HCO_3^- rapidly enough to meet the needs and has the possible advantage of being easy to prepare and nonirritating when given subcutaneously.¹⁰⁴ A greater dilution of physiologic saline solution by bicarbonate or lactate does not appear either necessary or desirable.

The calculation of the bicarbonate requirement, as sometimes done from the plasma carbon dioxide* and weight of the patient,^{89, 104, 105} involves the assumption that the bicarbonate contents of extracellular and intracellular fluids are equal. Since it has been shown that no such equality exists,^{106, 107} the calculation may involve a 50 per cent error and therefore is hardly worth while. Moreover, the amount of molar sodium bicarbonate that results in a given effect on the serum carbon dioxide has been shown to vary in different patients.¹⁰⁸ Physiologically it appears sounder to appraise the need of bicarbonate by careful clinical appraisal of the metabolic disturbance and respirations as indicated by the history and physical findings.

In appraising acidosis by hyperpnea it should be remembered that hyperpnea may be of central-

*Assuming that total plasma carbon dioxide per liter times 19/20 equals body fluid HCO_3^- per liter and that liters of body fluid equal kilograms body weight times 0.70.

nervous-system, not metabolic, origin. Primary hyperventilation of such origin, although resulting in a diminished total plasma or blood carbon dioxide, is associated with an alkalosis, not an acidosis.^{52, 70, 71, 73-77} The fifth diagram in Figure 1 depicts the plasma of a patient with primary hyperpnea and hence respiratory alkalosis. The HCO_3^- is diminished just as in the patient with the metabolic acidosis of diarrhea, but the pH is elevated and the patient is suffering from an alkalosis. This limitation in the diagnostic information provided by such a carbon dioxide determination is clearly illustrated by the diagrams of Figure 1. The second and third demonstrate that there can be either an alkalosis or an acidosis with an elevated HCO_3^- or total carbon dioxide. The fourth and fifth show that either an alkalosis or acidosis may be accompanied by a low HCO_3^- or total carbon dioxide. Similarly it should be noted that an alkalosis may be present with either a diminished or elevated serum Cl^- , as illustrated in the second and fifth diagrams. The significance of analysis of carbon dioxide or Cl^- depends on a proper correlation of the history and physical findings.

If the metabolic disturbance is a type that predisposes to acidosis, — for example, diarrhea or diabetic coma, — the degree of hyperpnea provides an index of the severity of the acidosis except in the premature, the newborn or the patient in shock.^{52, 72} Both the dehydration and acidosis are corrected by the infusion of a mixture of one part 1/7 molar sodium bicarbonate or lactate and two parts 0.85 per cent saline solution at the rate appropriate for hydration of the patient concerned — in other words, at the rate appropriate for the infusion of physiologic saline solution. The amount of this mixture infused is determined by the duration of the hyperpnea. Usually after one to two hours, when the gross hyperpnea has abated, physiologic saline solution may be substituted for the mixture of alkali and saline solution, since at such time the acidosis is no longer extreme and the extracellular hydration has so improved the blood flow and renal function as to permit the selective renal excretion of Cl^- above that of Na^+ and thus the elimination of the excess Cl^- of the saline solution.

The actual manner of estimating the parenteral extracellular repair therapy for an infant and for an adult suffering from acute nutritional failure with diarrhea, dehydration, acidosis and inability to take food and fluids orally is illustrated by the data of Table 1. The indicated repair therapy is of course provided in addition to the required maintenance needs, as stated in the previous article.⁶⁷

As already mentioned, the extracellular loss approximates one half the total weight loss or from 4 to 6 per cent of the patient's weight. The extracellular repair needs are easily provided by the intravenous or subcutaneous administration of

and of a mixture consisting of two parts of the former and one of the latter.

In Figure 1, the diagram of the plasma of a patient with gastric vomiting and excessive loss of chloride shows an abnormally low plasma chloride concentration. Ketone acids, which have accumulated as a result of the starvation, partially replace the loss in Cl^- . The HCO_3^- has increased to balance the Na^+ left uncovered by the Cl^- deficit. The history of gastric vomiting and the resulting elevation in HCO_3^- concentration above normal indicates a metabolic alkalosis. But it is important

trations resulting from gastric vomiting.^{52, 70, 71, 77, 87, 90, 100} The choice between 5 and 10 per cent dextrose depends on the amount of solution to be infused. In moderate dehydration, in which the rate of infusion is relatively slow and the total amount moderate, 10 per cent is required to meet the caloric requirements specified for maintenance needs, as noted in the previous article.⁶⁷ However, in severe dehydration, in which a more rapid initial rate of infusion is indicated to repair the dehydration, the initial use of 5 rather than 10 per cent dextrose in saline solution appears preferable to avoid

0.85 gm.% NaCl		M/7 NaHCO_3^*		2 parts 0.85 NaCl 1 part M/7 NaHCO_3	
+	-	+	-	+	-
Na^+	Cl^-	Na^+	HCO_3^-	Na^+	HCO_3^-
145	145	143	143	144	47
					Cl^-
					97

* Or M/7 Na-lactate

FIGURE 2. Diagrammatic Representation of the Electrolyte Composition of Physiologic Saline Solution, M/7 Sodium Bicarbonate Solution and a Mixture of Two Parts of the Former and One Part of the Latter. The figures represent milliequivalents per liter.

to note that without the history and physical findings the change in HCO_3^- concentration, as measured by the total carbon dioxide, could not establish such a diagnosis. Thus, although the plasma of a patient with emphysema (Fig. 1) had a similar increase in HCO_3^- and lowering of Cl^- ,^{70, 71, 73, 98, 99} the latter had an acidosis not an alkalosis. The determination of the serum pH, however, permits this differentiation by chemical means alone.

To treat the case of gastric vomiting, the infusion of 0.85 per cent saline solution, which contains no HCO_3^- and approximately one and a half times more Cl^- than plasma (Fig. 2), tends to increase the low plasma Cl^- , to decrease the elevated plasma HCO_3^- and thus to correct the hypochloremia and alkalosis. The simultaneous infusion of 5 or 10 per cent glucose limits the starvation and reduces the ketosis. Thus, 5 or 10 per cent dextrose in 0.85 per cent saline solution provides an initial parenteral-fluid therapy that is almost ideal for correcting the dehydration and disturbed plasma and extracellular fluid concen-

excessive hyperglycemia and glycosuria. The greater volume of fluid administered under such conditions of dehydration offsets the diminution in concentration.

The foregoing considerations indicate that the lack of HCO_3^- and the hypertonicity of Cl^- in physiologic saline solution relative to the Cl^- concentration of normal plasma (Figs. 1 and 2) render physiologic saline solution inappropriate as the initial parenteral therapy for correcting the disturbed plasma and extracellular fluid concentrations resulting from dehydration and acidosis. Inspection of the first and fourth diagrams in Figure 1 and the first diagram in Figure 2 should make this clear.

There is ample evidence^{87, 89, 101-103} that the infusion of 0.85 per cent saline solution in an acidotic dehydrated patient whose renal function is impaired by the dehydration, as evidenced by an elevated nonprotein nitrogen and other abnormal serum concentrations, may raise the plasma Cl^- above normal and thus prevent increase in the HCO_3^- and alleviation of the acidosis and hyperpnea. Before the

days when sterile sodium bicarbonate and sodium lactate solutions¹⁰⁴ were available, 10 per cent dextrose was added to the physiologic saline solution to so increase blood flow and improve renal function that the excess Cl^- could be excreted promptly.^{88, 95} The resulting increase in urine volume favored the urinary excretion of Cl^- , nonprotein nitrogen and other catabolites and the acidosis was ultimately corrected. Fortunately, sterile solutions of sodium bicarbonate or sodium lactate are readily available today. Therefore physiologic saline solution may be so diluted with these solutions that its hypertonicity in Cl^- is corrected and efficient hydration of the acidotic patient may be accomplished without delay in correcting the acidosis and hyperpnea. For example, the third diagram in Figure 2 depicts the concentrations obtained by diluting two parts of 0.85 per cent saline solution with one part of 1/7 molar sodium bicarbonate solution. Because this mixture has an HCO_3^- content almost double that of normal plasma, — that is, 48 milliequiv. per liter, — its infusion to a dehydrated acidotic patient with a low plasma HCO_3^- level and pH (fourth diagram Fig. 1) elevates the lowered plasma and extracellular bicarbonate and thus tends to correct the acidosis. At the same time, because the Na^+ and Cl^- concentrations of this mixture approximate those of normal plasma, it favors the restoration of normal serum Na^+ and Cl^- concentrations while repairing the deficit of extracellular electrolytes. One-seventh molar sodium lactate solution may usually be substituted for the NaHCO_3 solution, since the lactate ion appears to be oxidized to HCO_3^- rapidly enough to meet the needs and has the possible advantage of being easy to prepare and nonirritating when given subcutaneously.¹⁰⁴ A greater dilution of physiologic saline solution by bicarbonate or lactate does not appear either necessary or desirable.

The calculation of the bicarbonate requirement, as sometimes done from the plasma carbon dioxide* and weight of the patient,^{89, 104, 105} involves the assumption that the bicarbonate contents of extracellular and intracellular fluids are equal. Since it has been shown that no such equality exists,^{106, 107} the calculation may involve a 50 per cent error and therefore is hardly worth while. Moreover, the amount of molar sodium bicarbonate that results in a given effect on the serum carbon dioxide has been shown to vary in different patients.¹⁰⁸ Physiologically it appears sounder to appraise the need of bicarbonate by careful clinical appraisal of the metabolic disturbance and respirations as indicated by the history and physical findings.

In appraising acidosis by hyperpnea it should be remembered that hyperpnea may be of central-

nervous-system, not metabolic, origin. Primary hyperventilation of such origin, although resulting in a diminished total plasma or blood carbon dioxide, is associated with an alkalosis, not an acidosis.^{52, 70, 71, 73-77} The fifth diagram in Figure 1 depicts the plasma of a patient with primary hyperpnea and hence respiratory alkalosis. The HCO_3^- is diminished just as in the patient with the metabolic acidosis of diarrhea, but the pH is elevated and the patient is suffering from an alkalosis. This limitation in the diagnostic information provided by such a carbon dioxide determination is clearly illustrated by the diagrams of Figure 1. The second and third demonstrate that there can be either an alkalosis or an acidosis with an elevated HCO_3^- or total carbon dioxide. The fourth and fifth show that either an alkalosis or acidosis may be accompanied by a low HCO_3^- or total carbon dioxide. Similarly it should be noted that an alkalosis may be present with either a diminished or elevated serum Cl^- , as illustrated in the second and fifth diagrams. The significance of analysis of carbon dioxide or Cl^- depends on a proper correlation of the history and physical findings.

If the metabolic disturbance is a type that predisposes to acidosis, — for example, diarrhea or diabetic coma, — the degree of hyperpnea provides an index of the severity of the acidosis except in the premature, the newborn or the patient in shock.^{52, 72} Both the dehydration and acidosis are corrected by the infusion of a mixture of one part 1/7 molar sodium bicarbonate or lactate and two parts 0.85 per cent saline solution at the rate appropriate for hydration of the patient concerned — in other words, at the rate appropriate for the infusion of physiologic saline solution. The amount of this mixture infused is determined by the duration of the hyperpnea. Usually after one to two hours, when the gross hyperpnea has abated, physiologic saline solution may be substituted for the mixture of alkali and saline solution, since at such time the acidosis is no longer extreme and the extracellular hydration has so improved the blood flow and renal function as to permit the selective renal excretion of Cl^- above that of Na^+ and thus the elimination of the excess Cl^- of the saline solution.

The actual manner of estimating the parenteral extracellular repair therapy for an infant and for an adult suffering from acute nutritional failure with diarrhea, dehydration, acidosis and inability to take food and fluids orally is illustrated by the data of Table 1. The indicated repair therapy is of course provided in addition to the required maintenance needs, as stated in the previous article.⁶⁷

As already mentioned, the extracellular loss approximates one half the total weight loss or from 4 to 6 per cent of the patient's weight. The extracellular repair needs are easily provided by the intravenous or subcutaneous administration of

*Assuming that total plasma carbon dioxide per liter times 19/20 equals body fluid HCO_3^- per liter and that liters of body fluid equal kilograms body weight times 0.70

the saline and bicarbonate or lactate solutions. The intravenous administration is usually preferable because it results in less discomfort to the patient than administration by clysis and permits giving with the saline and sodium bicarbonate or lactate solutions the 5 or 10 per cent dextrose that is needed to provide the calories essential for the maintenance requirements.* In considering the administration of dextrose to the dehydrated acidotic patient, just as with the alkalotic one, 5 per cent dextrose appears preferable to 10 per cent in the initial parenteral therapy because the desirable rate of infusion in the initial phase of such therapy exceeds that at which 10 per cent dextrose can be administered without causing excessive hyperglycemia and glycosuria.

The application of these general principles to the initial parenteral therapy of the patient in diabetic coma is apparent. Because the literature is large and the issues somewhat confused, the parenteral therapy of such patients will be considered in a separate review of the therapy of diabetic coma.

INTRACELLULAR LOSSES AND REPAIR

Although the quantitative importance of intracellular losses incident to dehydration is evident,^{71, 79-84} little is known about their qualitative differences according to the manner of the dehydration and the occurrence of intracellular alkalosis or acidosis.^{106, 109}

Such transfusions of whole blood or plasma as are specified in Table 1 are given primarily to sustain red-cell and plasma volumes and plasma protein concentration. Some recent evidence indicates that plasma transfusions may be less effective in maintaining blood and plasma volumes than are whole-blood transfusions⁵³⁻⁵⁵; however, they provide some cellular nourishment, although the amount so provided is small. Recent observations concerning carbonic anhydrase¹¹⁰ suggest another advantage of whole blood over plasma. Carbonic anhydrase is an enzyme that accelerates the splitting of carbonic acid to form carbon dioxide and water. The enzyme is present in red cells¹¹¹ and is inhibited by serum.¹¹² The low concentrations of carbonic anhydrase observed in premature and newborn infants¹¹³ increase following transfusions of adult blood.¹¹³ Thus it has been suggested that whole-blood transfusions have a particular role in treating the acidosis and cyanosis of the newborn.¹¹³

Ringer's solution contains so few of the intracellular electrolytes that its administration accomplishes little more than giving an unwarranted feeling of satisfaction to the physician and causing expense to the hospital or patient. The provision of amino acids is included in the recommended maintenance therapy given in the first article.⁶⁷ The amounts specified barely cover normal main-

tenance requirements. In extremely depleted patients or patients sustaining severe nitrogen losses incident to burns⁷ or shock,^{6, 8-10} larger amounts of amino acids may be indicated.

But the addition of such intracellular parenteral therapy to the routine extracellular parenteral solutions does not provide the PO_4^{--} , K^+ , Mg^{++} and Ca^{++} that have been lost by these depleted patients and that are essential to a resumption of normal cellular metabolism. Therefore, until the present limitations in providing these substances parenterally are overcome, it is important to start oral feedings as soon as this can be accomplished without nausea or diarrhea.^{52, 89} Since adequate dextrose, extracellular constituents and intracellular crystalline enzymes or vitamins can be given parenterally, the oral feedings should provide readily digested foods, containing nitrogen, potassium, phosphate, magnesium and calcium. Beef broth, diluted milk and properly flavored amino acid preparations, if not nauseating, are suitable.

An acute nutritional disturbance, particularly in infants, is not infrequently accompanied by a diminution in gastric acidity and invasion of colon bacilli into the stomach. The dilution and acidification of fat-free milk with a lactate buffer (pH 3) has been advocated as a means of facilitating acid gastric digestion and restoring normal gastric acidity when milk feedings are started.¹¹⁴ Whether or not the sodium content of this buffer makes it superior to lactic acid appears to depend on the patient's need for extracellular base. Attention has recently been called to the possible danger of overacidification.¹¹⁵ The addition of ascorbic acid and members of the vitamin B complex to the oral feedings of depleted patients seems desirable.

It is frequently advantageous to start small oral feedings for intracellular repair before the parenteral fluid therapy is discontinued. In so doing some of the essential intracellular nutrients can be provided early with a minimal demand on gastrointestinal function. As the patient demonstrates an ability to handle the oral feedings, they are increased in amount and the parenteral fluids are eliminated.

CHECKING THE STATE OF THE PATIENT

Although careful observation of fluid intake, urine volume, number and volume of stools, respirations, pulse, temperature (including the extremities) and state of hydration by physical examination is essential and invaluable,⁵² adequate appraisal of the state of a previously depleted patient who has been nourished only by parenteral fluids for longer than twenty-four hours is difficult without the aid of chemical analyses of the blood. This is particularly true in the presence of continuing vomiting, diarrhea or the loss of gastric and intestinal juices by other routes.

Determination of whole-blood hemoglobin and the serum concentration of roten indicates the

*Although 5 per cent dextrose may be given subcutaneously in the dehydrated patient it not only may be absorbed very slowly but also may in the process of absorption remove extracellular fluid.^{82, 108}

of whole blood or serum, initially or in the course of parenteral-fluid therapy. Comparison of serial or daily hemoglobin and protein values reveals the trend in the patient's water balance and need of fluid.^{68, 69} The relative adequacy of renal excretion and function may be appraised by determining the nonprotein nitrogen concentration. The presence of chloride depletion with increased serum CO_3^- concentration, alkalosis and the need of physiologic saline solution, or the presence of base deficit with a decreased serum HCO_3^- level, acidosis and the need of the combination of sodium carbonate (or lactate) and saline solution, may be determined initially or checked during therapy by analyses of the serum concentrations of chloride and either sodium or carbon dioxide. However, as already mentioned, a careful interpretation of the laboratory and clinical findings is necessary before the carbon dioxide content of the serum can be used as an index of alkalosis or acidosis. Indeed, a critical appraisal that permits interpretation of the carbon dioxide concentration usually means that the actual determination of the carbon dioxide attributes but confirmatory information. The presence of acidosis or alkalosis may be definitely established by determining the serum or whole-blood pH.

The amounts of blood or serum required for these analyses are as follows: hemoglobin, 0.02 cc of whole blood¹¹⁶; serum protein, 0.02 cc.¹¹⁷; non-protein nitrogen, 0.1 cc. of whole blood or serum¹¹⁸; serum chloride 0.5 cc.¹¹⁹; serum sodium, 0.5 cc.¹²⁰; serum carbon dioxide, 0.5 cc.¹²¹; and pH, 0.2 cc.¹²²

SUMMARY

The parenteral therapy of the patient unable to take fluids or food by mouth has been reviewed. The first part of this review outlined the estimation of maintenance requirements and the provision of maintenance therapy under the separate categories of water, sodium chloride, nitrogen and calories. In the second, part considers the estimation of the losses incident to starvation and dehydration and the provision of repair therapy. It specifically deals with the clinical appraisal of the dehydration and the accompanying acidosis or alkalosis; extracellular losses and their repair; intracellular losses and repair; and checking the state of the patient and his needs by blood analyses.

The importance of providing the therapy described under all these categories is emphasized. It is hoped that this manner of review provides physiologic concepts and therapeutic measures that may be integrated by the physician to meet the needs of each patient.

The data tabulated under each category are applicable to the parenteral therapy of infants, children and adults. The requirements of sodium chloride for maintenance and for repair are reviewed separately to emphasize their different orders

of magnitude. Appreciation of this difference should avoid oversalting the patient requiring only maintenance therapy and undersalting the patient requiring extensive extracellular repair therapy. The possible need of providing 10 to 15 per cent dextrose in maintenance parenteral therapy where relatively moderate total volumes of solution are infused at a slow rate is indicated. On the other hand, where a larger volume of repair solution is being rapidly infused in the initial therapy of severe dehydration, a concentration of 5 per cent dextrose in the parenteral fluid appears to provide a total amount adequate to meet the caloric requirements. The suitability of using 0.85 per cent saline solution in the parenteral therapy of the dehydrated alkalotic patient is described. The inappropriateness of such a solution in the initial parenteral therapy of the dehydrated acidotic patient and the desirability of substituting a mixture of one part 1/7 molar sodium lactate or bicarbonate solution and two parts physiologic saline solution are emphasized. The simplification of thought concerning disturbances in water and electrolyte balance provided by utilization of the milliequivalent as the unit of concentration is illustrated.

Attention is called to the importance of intracellular losses in dehydration and starvation and to the inadequacy of present-day parenteral therapy to repair such losses. The administration of appropriate food orally early during the course of therapy is emphasized.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30441

PRESENTATION OF CASE

A seventy-nine-year-old man entered the hospital for study.

For many years before admission the patient complained of urinary symptoms, including frequency and nocturia (six to eight times). There was diminution in the caliber and strength of the urinary stream, with dribbling and intermittency of urination. Six years prior to entry he was told that he had "prostatic trouble." During the few months before admission his urinary difficulties increased in severity.

*On leave of absence.

The past history revealed that the patient had a moderate tremor of the extremities for thirty years and of the head and voice for two years.

Physical examination revealed a well-developed and well-nourished man in no obvious distress. There was bilateral arcus senilis. There was a gross tremor of the head. The chest was moderately emphysematous. The lungs were clear to auscultation and percussion. The heart was slightly enlarged to the left on percussion. The rhythm was normal. There were no murmurs or thrills. Multiple extrasystoles were heard over the apex. The abdomen was negative, except that the bladder was distended, reaching to 5 cm. below the umbilicus. The prostate was twice the normal size, nontender, resilient and movable. There were marked tremors of the extremities and of the voice. Neurologic examination was negative.

The blood pressure was 240 systolic, 104 diastolic. The temperature was 98.6°F., the pulse 80, and the respirations 20.

Examination of the blood showed a red-cell count of 4,750,000, with a hemoglobin of 85 per cent. The white-cell count was 9400. The urine showed a + to +++ test for albumin; the sediment contained innumerable red cells, and a culture revealed abundant *Staphylococcus albus*. The nonprotein nitrogen was 35 mg. per 100 cc.

An x-ray film of the chest showed a slight amount mottled, increased density in the left upper lobe and the first interspace. The bases of both lungs were emphysematous. There was a rounded area of calcification 1 cm. in diameter at the right base, which was thought to represent a Ghon lesion. The diaphragm was low in position. There was no prominence of the left ventricle, but the thoracic ratio was 14:30. An intravenous pyelogram was negative.

On the third day the patient suddenly complained of severe, nonradiating subxiphoid pain accompanied by slight nausea and, two hours later, vomiting. Physical examination revealed an occasional extrasystole in a slightly enlarged heart, with otherwise regular rhythm. There were a split mitral second sound and a faint apical systolic murmur. The lungs were clear. There was no evidence of cardiac failure, and the patient was not cyanotic. The epigastrium was not tender. The legs were normal. The blood pressure was 260 systolic, 120 diastolic. The patient was confined to bed and given 11 mg. ($\frac{1}{4}$ gr.) of morphine. The pain lasted two hours and then subsided.

Two days later an electrocardiogram revealed a normal rhythm, with a rate of 60, a PR interval of 0.17 second, a slightly sagging ST segment, an upright T_1 , a low upright T_2 and a small Q_2 (2 mm.) and Q_3 (3 mm.), with deep late inversion of T_2 ; the precordial leads showed upright T waves, with slightly sagging ST segments in CF_4 and CF_5 . The blood pressure was 150 systolic, 60 diastolic. The corrected sedimentation rate was 1.8 mm. per minute.

An electrocardiogram taken on the seventh day after admission revealed a normal rhythm, with a rate of 60, a PR interval of 0.17 second, sagging ST_1 and ST_2 , an upright T_1 , diphasic T_2 and T_3 and small Q_2 and Q_3 ; the precordial lead showed an upright T wave. An electrocardiogram taken fourteen days after admission showed normal rhythm, with a rate of 80, a PR interval of 0.16 second, an upright T_1 , a flat T_2 , an inverted T_3 , small Q_2 and Q_3 , slight slurring of QRS_2 and an upright T in the precordial leads.

In the meantime, beginning with the fifth hospital day, the patient began to run a low-grade fever. The lungs were clear. There was slight tenderness at the costovertebral angle. Urinalysis revealed a sediment containing innumerable white cells. A urine culture showed abundant colon bacilli and hemolytic streptococci. A blood culture was negative. On the fourteenth hospital day the patient was put on a course of 0.5 gm. of sulfathiazole every eight hours. He continued to run a temperature of 102°F., but the lungs remained clear, except for a few fine rales at the right base posteriorly. The legs were normal.

A chest plate taken on the twentieth hospital day revealed a large amount of fluid in the posterior

costophrenic angle on the right. On the following day bilateral superficial femoral-vein ligations were done. No clots were found. On the twenty-first hospital day the nonprotein nitrogen was recorded as 38 mg. per 100 cc. The white-cell count was 26,600. The patient complained of pain above the symphysis pubis. The pulse rate was 116, with an occasional dropped beat. The chest showed a few rales, slight dullness and decreased fremitus in the left base posteriorly. The abdomen was somewhat distended. He became weaker, drowsier, went into Cheyne-Stokes respiration and had frequent episodes of vomiting.

On the twenty-sixth hospital day the nonprotein nitrogen was 86 mg. per 100 cc. in spite of an excellent fluid intake and a good urinary output. The electrocardiogram showed a rate of 140, a PR interval of 0.14 second, a sagging ST_1 , an upright T_1 , a sagging ST_2 , an upright T_2 , a low upright T_3 , a wide slurring of QRS_2 , small Q_2 and Q_3 , an upright T in CF_2 , CF_4 and CF_5 , and a sagging ST in CF_4 . A chest plate revealed less fluid in the pleural cavity. There was moderate pitting edema of both feet, in spite of digitalis and restriction of salt. The patient continued to have abdominal distention and episodes of vomiting.

On the thirty-fourth hospital day he exhibited pitting edema of the hands, arms, legs and sacrum. The total protein was 4.3 gm., and the nonprotein nitrogen 52 mg. per 100 cc. Five days later he suddenly complained of severe precordial constriction, without radiation. Physical examination revealed a tachycardia and a scratchy systolic murmur, loudest at the left border of the sternum. The lungs were clear anteriorly and laterally. The patient was not dyspneic or cyanotic. The neck veins were not distended, nor were they pulsating. An electrocardiogram showed a sinus tachycardia of 150, a PR interval of 0.13 second, sagging ST_1 and ST_2 , a low T_1 , an upright T_2 and T_3 , and a sagging ST in CF_4 and CF_5 , with low upright T waves. Six hours after the onset of this attack, on the fortieth hospital day, the patient expired.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: This patient was so old that anything could have been wrong with him. He was not acutely ill at first. He came to the hospital for a urologic check-up.

"The heart was slightly enlarged to the left on percussion," a difficult method of examination in the presence of pulmonary emphysema. X-ray study was certainly in order to determine the true size of the heart.

"The prostate was twice the normal size, nontender, resilient and movable." I do not know whether that rules out malignancy, but I believe that it is evidence against it.

There was some hypertension, largely of the arteriosclerotic type, with relatively low diastolic

pressure, as diastolic hypertensions go. The patient had an extremely high systolic pressure for a time; later it came down. There was a pulse pressure of over 100 mm.

There was hematuria, but not much evidence of severe renal infection at that time. Was more than one culture made? There is a strong suspicion of infection, which may have been renal.

What was the specific gravity of the urine?

DR. BENJAMIN CASTLEMAN: The specific gravity was 1.022; following this it was 1.030, and then 1.012, 1.010 and 1.008.

DR. WHITE: There was evidently good concentration, which is of considerable importance.

DR. CASTLEMAN: Only on admission. After the first week it was in the neighborhood of 1.012 and 1.010.

DR. WHITE: "On the third day the patient suddenly complained of severe, nonradiating, subxiphoid pain accompanied by slight nausea and, two hours later, vomiting." Except for the hypertension, this is where the cardiovascular part of the case comes in.

The split mitral second sound was probably not significant, unless interpreted as a gallop rhythm, which was not at all definite and rather unlikely. If we are looking for trouble below the diaphragm, from the standpoint of an abdominal emergency, nausea and vomiting fit in of course; they are not so frequent with cardiovascular accidents but can occur. Also, one must think of the possibility of pulmonary embolism from phlebitis. The legs were, however, said to be normal. The pulse presumably was definitely felt in the feet.

The blood pressure went up under the stimulus of this pain. That sometimes happens, no matter what the fundamental cause may be; it drops only with great prostration and collapse.

We should not make too much of the electrocardiogram, and yet it may give important clues to explain an acute process. The findings here could have been due to a fresh posterior myocardial infarct, three days old. If a record had been taken on the first or second day, perhaps there would have been more evidence of change in the ST segment if a fresh myocardial infarct had occurred. The tracing is not characteristic of acute cor pulmonale in that there is no S wave in Lead I.

DR. CASTLEMAN: The electrocardiogram was taken forty-eight hours after admission.

DR. WHITE: It was taken reasonably soon after the attack, but the changes would have been more definite in the first twelve hours, especially in the precordial leads. The precordial T wave is high if anything, which helps to rule out an acute cor pulmonale and favors a posterior myocardial infarct. The sagging of the ST segments in Leads CF₄ and CF₆ is also in keeping with that, although it did not last long. The small Q waves are unimpressive.

There was a drop in blood pressure forty-eight hours after the attack.

Another electrocardiogram showed a more pronounced inversion of the T waves in Lead 2 and Lead 3. T₂ is not so deep as before, but there is a greater change in Lead 2, the precordial T waves still being upright, although not so strikingly high. The very height of these T waves makes one think of the possibility of posterior myocardial infarction, for an extremely high T wave is often as significant as an inverted T wave.

There was not a great deal of change in the third electrocardiogram according to the description, mostly a straightening out of the waves; T₂ was flat, and T₃ inverted, although not so deep, again with high T waves in the precordial leads.

How high was the temperature two days after the attack and how high did it go?

DR. CASTLEMAN: It went to 103°F. at one time.

DR. WHITE: That is a fair degree of fever for myocardial infarction alone; in fact, it is higher than one would expect. The lungs were clear, and there was slight tenderness in the costovertebral angle. Urinalysis revealed a sediment containing innumerable white cells. Apparently there was a pyuria. The urine culture showed abundant colon bacilli and streptococci. Much of the fever may have been due to infection in the genitourinary tract.

The patient was put on sulfathiazole, evidently to combat this urinary infection. Probably his physicians thought that the fever was due to infection rather than to the process that was responsible for the substernal pain.

"The legs were normal." They were still looking hard for a source of embolism.

In addition to the information about the chest I should like to know how large the heart was and about the aorta, because in some of these accidents we have to think of dissecting aortic aneurysm, which may involve the renal circulation.

DR. LAURENCE L. ROBBINS: These are the films referred to first. There is a small amount of fluid in the posterior costophrenic angle. The shadow that appears to be within the lungs possibly represents a small area of infarction. In subsequent films, there is rather marked change in the appearance of the vascular shadows in the lung fields. They have increased in size. I cannot be sure of the heart measurements because the film was taken to demonstrate the lung fields rather than the heart. This film gives a fairly accurate idea of the size of the heart. There is no enlargement, but there is evidence of left ventricular hypertrophy.

DR. WHITE: Was that taken before the attack?

DR. ROBBINS: Yes.

DR. WHITE: Despite the systolic hypertension, the heart was not particularly large for a patient of seventy-nine; evidently he supported the systolic

hypertension extremely well, but we do not know how long he had had it.

DR. ROBBINS: There does not appear to be much increase in the size of the heart. In this film, taken later, there is evidence of an increase in pulmonary congestion, and the shadow seen in the previous film is obscured by a high diaphragm.

DR. WHITE: It looks as if there were less fluid.

DR. ROBBINS: I am not certain about the amount of fluid because the film was taken with the patient on his back, and the diaphragm is higher than in the previous films. There might be some fluid.

DR. WHITE: The report says there was "less pleural fluid."

DR. ROBBINS: That is true, but if the fluid gravitated posteriorly in the chest one would see a sharp costophrenic angle and not much fluid.

DR. WHITE: There must have been strong clinical evidence of pulmonary embolism or infarction, since the leg veins were ligated.

The leukocytosis was too high for an infarct of the heart or lung without complications. I think that this indicates that more than one thing was wrong; the genitourinary complication doubtless enters in here.

Is there indication of fluid in the left base?

DR. ROBBINS: No.

DR. WHITE: The patient then became uremic.

The PR interval decreased, characteristic of an increased heart rate, and T₁ came back to a more normal appearance. There is no apparent evidence of a fresh myocardial infarction.

"The total protein was 4.3 gm." That, as well as the renal state, may account for part of the edema.

"He suddenly complained of severe precordial constriction without radiation." Apparently this was not the same as the pain that occurred several weeks previously. It was again precordial, however, although not necessarily substernal; there was constriction. I wonder if he was dyspneic at that time; there is no statement to that effect.

I also wonder whether the pericardial friction rub might have been the result of uremia or of a distended right ventricle and pulmonary artery following pulmonary embolism. There was no evidence of heart failure at that time to explain the fluid in the chest.

In summary, the patient certainly had prostatic hypertrophy and obstruction, quite mild, with retrograde infection of the urinary tract, including pyelitis and terminal uremia. I shall hazard a guess that he had pericarditis resulting from uremia. There was also hypertension, of the systolic type, not causing much cardiac enlargement originally; there was slight left ventricular enlargement, with increase in size of the heart, after the first acute episode, which I shall interpret as posterior myocardial infarction. I shall add to that a diagnosis of terminal pulmonary embolism and infarction —

in these older patients, the more diagnoses the better. Also there was anasarca due to a combination of several factors — renal disease, hypoproteinemia and, perhaps, heart failure.

DR. CONGER WILLIAMS: This patient was on our service last month. I thought that the first episode probably represented myocardial infarction. His veins were tied because there was a suspicion of pulmonary infarction and we thought that it could do no harm. Later many things developed, including terminal uremia. When the final episode started was of no more than academic interest because of other things that had occurred; I thought that the last episode was suggestive of pulmonary embolism, even though the veins had been tied off. Such a thing does happen.

DR. WHITE: The first attack was different from the second?

DR. WILLIAMS: I did not see the patient in the last attack, but as it was described to me it sounded as if it were due to pulmonary embolism.

DR. HOWARD B. SPRAGUE: Do you think that he had a pulmonary embolus that arose in the right heart following the basal infarct?

DR. WHITE: Such a condition is rare.

DR. SPRAGUE: I know it, but I recently had a case.

DR. WHITE: It is possible, but I should not make that diagnosis.

CLINICAL DIAGNOSES

Benign prostatic hypertrophy.
Chronic pyelonephritis.
Uremia.
Old pulmonary infarct with bilateral vein ligations.
Recent myocardial infarction?

DR. WHITE'S DIAGNOSES

Prostatic hypertrophy and obstruction.
Pyelitis.
Uremia.
Pericarditis, uremic.
Hypertension, with slight cardiac hypertrophy.
Posterior myocardial infarction.
Hypoproteinemia.
Anasarca.
Pulmonary embolism and infarction, terminal.

ANATOMICAL DIAGNOSES

Myocardial infarction: left ventricle and posterior part of septum.
Interstitial myocarditis and generalized perivascular cellular infiltration (sulfonamide idiosyncrasy).
Cardiac hypertrophy, hypertensive type.
Pyelonephritis, acute and chronic.
Prostatic abscesses.

Adenocarcinoma of prostate.
Cystitis.
Hydrothorax, bilateral.
(Uremia.)

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed an enlarged heart, weighing 420 gm., of the hypertensive

the neoplasm around nerves, and no evidence of metastasis anywhere in the body.

Microscopic sections of the heart showed, first, the obvious infarct of almost a month's duration. Sections away from the infarct and corresponding to the location of the pinpoint grayish-red areas observed grossly showed an interstitial myocarditis. There was a cellular infiltration, consisting mostly of eosinophils and monocytes, in the interstitial

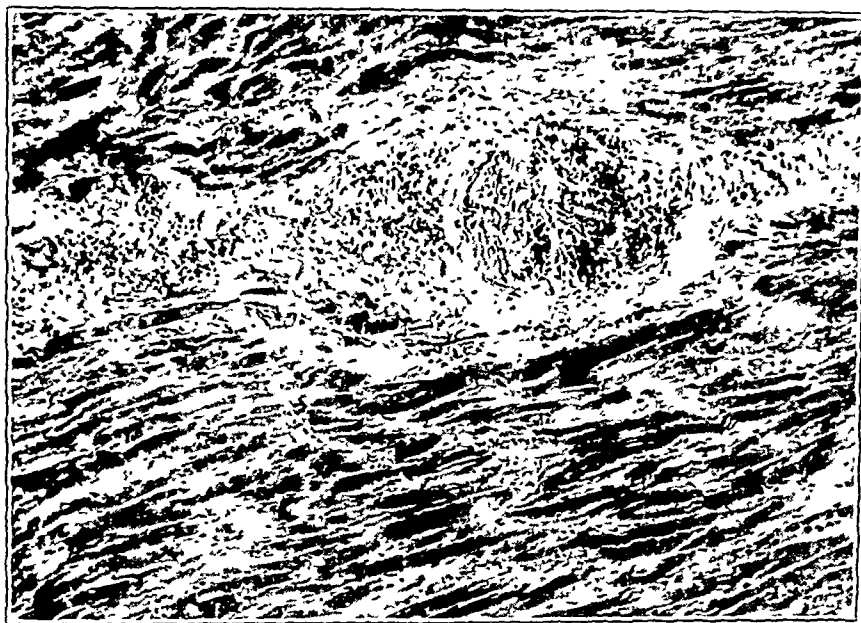


FIGURE 1. Photomicrograph of Section of Heart Muscle.

type, the hypertrophy being left ventricular. In the right coronary artery, 9 cm. from its origin, we found an occluding recent organizing thrombus, the age of which would fit in with the time of the attack that he had had on the third hospital day. The circumflex and descending branches of the left coronary artery were markedly sclerotic, but there was no evidence of occlusion.

The myocardial infarction was limited to the posterior wall of the left ventricle, although there were some tiny grayish-red areas in other parts of the heart that we could not explain. There were no infarcts in the lung, and no evidence of pulmonary emboli.

There was 500 cc. of fluid in each chest cavity, but none in the abdomen.

Both kidneys were markedly enlarged and swollen, and we thought that grossly they suggested a pyelonephritis. The bladder showed a mild cystitis. The prostate was enlarged to twice the normal size, showing considerable necrosis and infection. In one area there was a small but definite adenocarcinoma. There was no evidence of extension of

tissues, especially around the blood vessels (Fig. 1). These findings are quite similar to those of interstitial myocarditis due to sulfonamides, first observed by French and Weller.¹ Similar perivascular infiltrations were found in the lungs (Fig. 2) and in one section of smooth muscle. I believe that these changes followed the sulfonamide therapy, apparently a hypersensitivity reaction. Perhaps this is the early stage of the frank periarteritis that has been described by Rich.² There were similar areas in the kidney, but one cannot be sure that they were due to sulfonamides. The patient had a severe pyelonephritis, and they can be explained on that basis. In a case of severe sulfonamide nephrosis, which we discussed here a year ago,³ the myocardium showed exactly the same picture—eosinophilic, lymphocytic and monocytic infiltration in the interstitial tissues and around the vessels.

It is quite possible that some of the changes in the electrocardiogram may have been due to these lesions. Dr. Bernard Maisel, who worked in our laboratory a year or so ago on sulfonamide intoxications, has just told us about a patient who

received sulfonamides prophylactically before an intestinal resection for carcinoma and who after the operation developed signs of cardiac failure with queer electrocardiographic changes; at autopsy the myocardium showed severe interstitial myocarditis.

DR. WHITE: In this case, some of the later changes did not fit in with the myocardial infarct, although

DR. CASTLEMAN: Yes.

DR. WHITE: Hence, congestive heart failure might have accounted for some of the fluid in the chest.

REFERENCES

1. French, A. J., and Weller, C. V. Interstitial myocarditis following clinical and experimental use of sulfonamide drugs. *Am. J. Path.* 18: 109-121, 1942

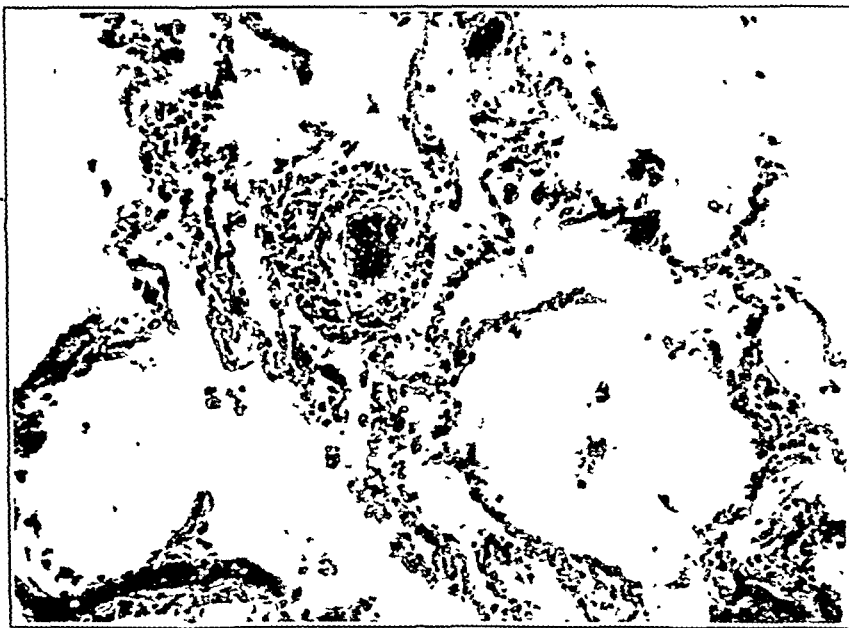


FIGURE 2. Photomicrograph of Section of Lung.

there was clear evidence thereof in the first few. It is conceivable that the sulfonamide myocardial changes might have altered the electrocardiogram, but we need more information to be certain.

Was the heart dilated?

2. Rich, A. R., and Gregory, J. E. Experimental demonstration that periarteritis nodosa is manifestation of hypersensitivity. *Bull. Johns Hopkins Hosp.* 72: 65-88, 1943
3. Case records of the Massachusetts General Hospital (Case 29211). *New Eng. J. Med.* 228: 687-690, 1943

CASE 30442

PRESENTATION OF CASE

A forty-three-year-old railroad worker was admitted to the hospital with pain in the region of the left costovertebral angle.

The patient was apparently in good health until two years prior to admission, at which time he had an attack of severe stabbing pain in the region of the left costovertebral angle, radiating to the left groin. Similar attacks, each lasting a few seconds, recurred at intervals of once or twice a week. He developed urinary frequency of about six to seven times daily and twice nightly. He also had pain and discomfort in the right upper quadrant, as well as abdominal distention at times. There was no jaundice, nausea or vomiting. One month prior

to admission the attacks increased in frequency and severity, occurring daily. At no time did he notice hematuria or pyuria, nor did he pass any gravel. He had lost 14 pounds over a period of six months. Because of his symptoms he visited the out-patient department of another hospital, where urograms were taken. These showed a huge left hydronephrosis with multiple calculi in the pelvis and calyces and no function. The right kidney was poorly visualized but was apparently normal in outline and pattern.

Except for the fact that the patient had been consuming four to five quarts of alcohol weekly over a period of five to six years, the past and family histories were noncontributory.

Physical examination revealed a well-developed man who appeared chronically ill. The heart and

lungs were normal. The left kidney was readily palpable, and left costovertebral angle tenderness was present. The spleen could not be felt.

The blood pressure was 130 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 3,350,000, with 60 per cent hemoglobin, and a white-cell count of 12,500. A voided specimen of urine had a specific gravity of 1.010, with a ++ test for albumin and many red and white cells in the sediment. The blood nonprotein nitrogen was 26 mg., the sugar 123 mg., the calcium 10.7 mg., and the phosphorus 4.4 mg. per 100 cc. The alkaline phosphatase was 2.4 units per 100 cc. The prothrombin time was 14 seconds (normal, 18 to 20 seconds). The serum protein was 6.9 gm. per 100 cc., with an albumin-globulin ratio of 1.4. A urine culture showed a few colonies of *Staphylococcus albus* and diphtheroids.

An intravenous pyelogram revealed numerous areas of calcification overlying the left kidney, which was not well visualized. No dye appeared on the left over a period of twenty minutes. The outline of the right kidney was normal, and the dye appeared promptly.

On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FLETCHER H. COLBY: The significant points in the history of this patient are the intermittent attacks of left costovertebral pain over a two-year period, which radiated to the groin at the outset. There was moderate frequency of urination, but no gross hematuria; and no stones were passed. Prior to admission the frequency increased and there was considerable loss of weight. Urograms were said to have been taken at another hospital that demonstrated a huge left hydronephrosis with multiple calculi; since this kidney undoubtedly had no function at that time, a retrograde pyelogram must have been done to visualize the renal pelvis.

The history suggests, of course, left renal colic, with stones as the likeliest cause. Such symptoms, however, may be due to other conditions, such as renal tumor, usually associated with the passage of blood clot, and various obstructive congenital lesions. Gastrointestinal symptoms are frequently produced by a fairly advanced lesion of the kidney, because of pressure on neighboring organs from a large renal mass or possibly reflexly through the sympathetic nervous system.

On physical examination the left kidney was sufficiently enlarged to be readily felt and there was left costovertebral angle tenderness. Moderate anemia was present. The urine was low in specific gravity and contained both blood and pus. The blood chemical findings, with normal calcium, phosphorus and protein determinations, appear to eliminate parathyroid disease. *Staph. albus* and diphtheroids

were found in the cultured urine. The diphtheroids are contaminants, but the staphylococcus is probably significant since some strains of this organism invade the urinary tract and are capable of separating urea, thus favoring stone formation by the strongly alkaline urine that is produced.

At x-ray examination the many areas of calcification are typical of stones scattered throughout a dilated, badly damaged, functionless left kidney. There is no good reason to suspect tumor from the evidence we have, although there is no method of eliminating this possibility. Tuberculosis is seldom associated with such extensive stone formation. One of the congenital abnormalities may have been the background for the renal damage and stone formation, but again we have no definite evidence of this. The operation performed on the fifth day was presumably a left nephrectomy for a calculus pyonephrosis. The appearance of the stones by x-ray suggests that they were composed of calcium phosphate.

CLINICAL DIAGNOSES

Nephrolithiasis.

Pyonephrosis.

DR. COLBY'S DIAGNOSES

Nephrolithiasis.

Pyonephrosis.

ANATOMICAL DIAGNOSES

Nephrolithiasis.

Pyonephrosis.

Carcinoma in situ and epidermoid carcinoma of renal pelvis, multiple.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This case was used in these exercises to illustrate one of the extremely rare conditions occurring with renal stones. As Dr. Colby predicted this patient did have a large pyonephrotic fluctuant kidney, with obliteration of most of the parenchyma by the dilated calyces (Fig. 1). There were several large stones within the pelvis and calyces. The unusual finding was the presence of several grayish-white, slightly raised, granular areas about 2 cm. in diameter on the mucosal surface of the pelvis and some of the calyces. In a few places these apparent tumors extended into the parenchyma. In other areas the mucosa was merely roughened.

Microscopic examination revealed all stages in the development of epidermoid carcinoma. The slightly roughened areas showed a marked atypicality and anaplasia of the epithelium but no evidence of invasion — a condition that we call "carcinoma in situ" (Fig. 2). Other areas showed early invasion with extensive keratinization — a Grade I epidermoid carcinoma (Fig. 3). In the grossly invading foci the carcinoma was a bit less differentiated and might be classified Grade II or III.

Although it cannot be proved, the presence of

multiple foci of carcinoma in all stages of development dated the neoplasm. It therefore seems reasonable

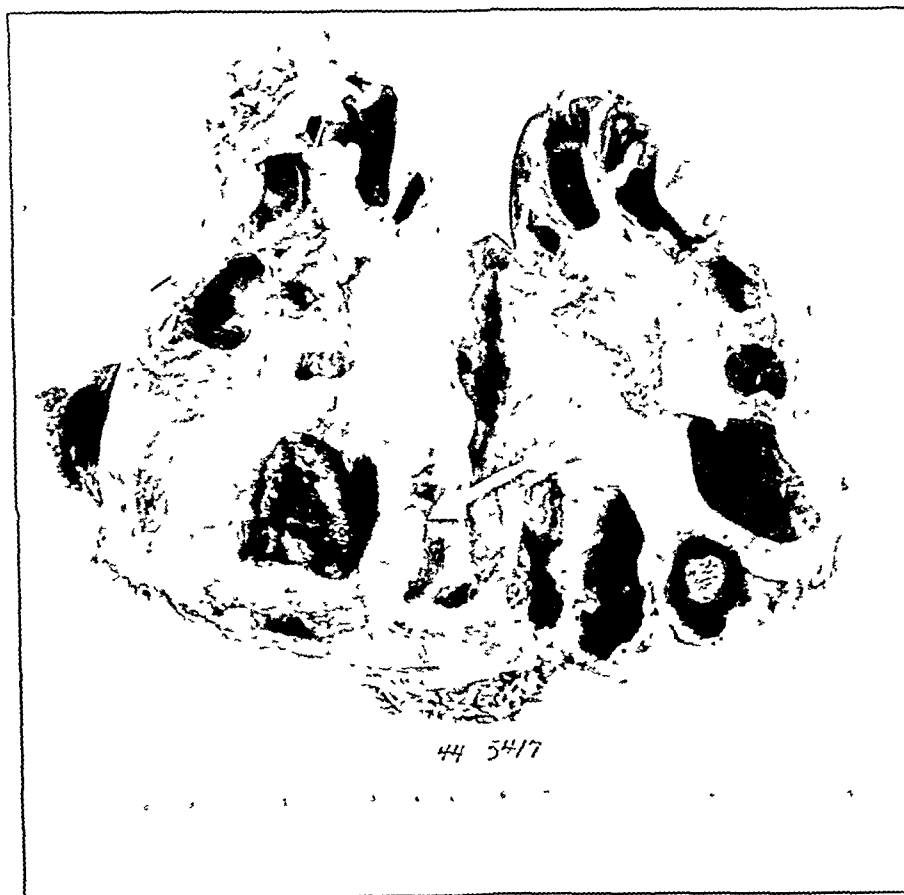


FIGURE 1. *Photograph of the Bisected Kidney.*
The arrow points to one of the granular areas mentioned in the text.

ment associated with multiple renal stones suggests that the chronic irritation of the calculi led to the

that the continued irritation of the stones and the infection had a great deal to do with the formation



FIGURE 2. *Photomicrograph of a Section of the Kidney.*
This area shows carcinoma in situ of the pelvic epithelium.

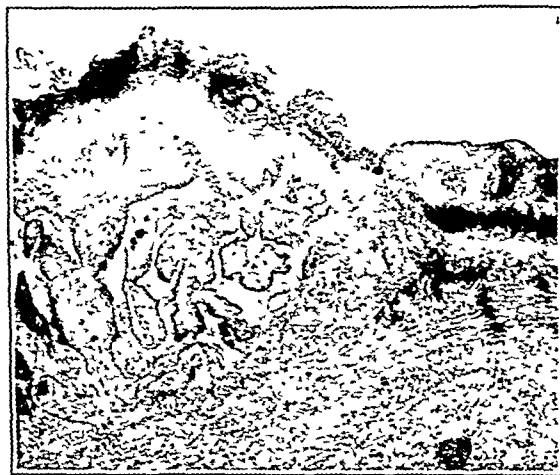


FIGURE 3. *Photomicrograph of a Section of the Kidney.*
This area shows epidermoid carcinoma of the renal pelvis.

formation of the neoplasms.

DR. COLBY: The curious appearance of the kidney certainly suggests that the stone formation ante-

of the carcinoma. There have been a sufficient number of similar cases reported in the literature to support this point of view.

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UNITED WAR FUND

FROM now until November 23 the Greater Boston United War Fund will be holding its campaign to raise \$7,650,000 for home-front and war-related appeals.

On meeting the home-front needs depends the physical and social health of the community. Two hundred and sixty-seven hospitals, clinics, dispensaries and youth and social services are affiliated with the Fund. Physicians need not be told of the work these services do; indeed, physicians give generously of their time and energy to serve the health of the community, and day after day see for themselves the needs of those whom they and these agencies serve.

In a world seething with hate and killing, our own community is only a small part of our responsibility. Every contribution to the Greater Boston United War Fund is also a direct gift to some homesick soldier or weary sailor overseas. We give to our men in uniform when we give to the USO, the United Seamen's Service, the War Prisoners Aid and the American Field Service. The needs of these men will not be immediately decreased when the European phase of the war ends, for the repatriation of prisoners will take a long time, large armies of occupation must be kept, and the problem of morale will increase. Then, too, our efforts in the Pacific will be increased, and these services must be ready for still larger tasks on the other side of the world.

Not less important are those who have suffered far more and far longer than any of us. United Nations Relief goes to sixteen war-ravaged countries, whose occupants have borne the brunt of the fight.

For our own neighbors, our fighting men and our brave allies, give and "Show That You Care."

NEED FOR REORGANIZATION

ALTHOUGH, by and large, during the last two years the people of the United States have not truly suffered from the lack of medical, nursing and hospital care, a number of situations have arisen that have already resulted in the lowering of standards of which this country had just reason to be proud. Furthermore, it seems likely that many, if not all, of these blunders might have been avoided if a broader and more knowledgeable attitude had been taken regarding the demands for medical and nursing personnel by the Army and Navy, particularly the former.

The men in the armed forces deserve the best of medical care, — and this they are undoubtedly receiving, — but unlike butter, the physician and the nurse are commodities that the civilians, the majority of whom are contributing in one way or another to the war effort, cannot do without. To cut down below a certain level, as well as to accelerate medical education, creates conditions that eventually undermine the health of the population. Already there is a shortage of hospital beds that

might be catastrophic in the event of a nationwide epidemic, and the average number of days of hospitalization has been prolonged, both of which are largely due to a depleted medical and nursing personnel. Medical-school graduates, to say nothing of faculty members, are tired and confused by three years of accelerated teaching, and hospitals obviously cannot give adequate practical training during a nine-month rotating internship or under the 9-9-9 plan. Finally, deferment has been denied to premedical students at a time when the number enrolled under the Army and Navy training programs has been drastically cut; this can only result in a diminution in the number of properly qualified students.

The educational aspect is forcefully brought to the attention of the medical profession by Dr. Evarts A. Graham in an editorial published in the August issue of *Surgery, Gynecology and Obstetrics*, which reads as follows:

The medical schools and civilian teaching hospitals of this country are engaged in the education of medical officers for the armed services. . . . That the efforts of the medical schools and teaching hospitals have been successful is attested by the extravagant praise accorded, especially, to the surgeons in the Army and Navy for the astonishingly high percentage of wounded men returned to active duty. . . .

The surgeons who are responsible for this splendid record are men who not only had the benefit of four years in a medical school following a good premedical training in the colleges but in addition spent several years in special training in our civilian teaching hospitals. Many also have fulfilled the requirements for fellowship in the American College of Surgeons and for certification by the American Board of Surgery. . . . The Army has recognized the importance of [such] qualification . . . by giving a certain amount of preferential consideration to the members of the College and particularly to those who hold certificates of the American Board.

This splendid plan, however, . . . has been scrapped by the War and Navy Departments. Laymen . . . have dictated what may be given in a premedical course, have streamlined the medical course itself and have practically destroyed the resident system of training. Many medical officers will now enter the army to serve in battalion aid stations and in other places demanding a knowledge of surgery whose maximum graduate hospital experience has been nine months of a rotating intern service with perhaps only two months in surgery. Is this the kind of medical officer the armed forces want? Pity the wounded if it is!

Let us imagine a group of surgeons with the authority to prescribe the education of line officers, be they Army or Navy. Would they wreck West Point and Annapolis? Would they reduce their faculties by 40 or 50 per cent at the same time that they increase the number of the students? Would they reduce the period of training of artillery

officers or submarine commanders to an amount which could not possibly make them efficient? It seems unlikely that they would. . . .

Is the medical officer of less value than the line officer? The General Staff may think so, but we know full well that a modern army could not function at all without its medical department. . . .

Although the Surgeon General . . . is no longer a member of the General Staff, the Army must appreciate the value of the medical officers because it wants so many of them even if they are only half-baked. In fact much of the present difficulty arises because of the large number wanted. At the outbreak of the present war we were told that the army needed 6.5 medical officers for each 1000 men in the Army. . . .

The demand for so large a number of medical officers is the fundamental cause of the disruption of the prewar efficient plan for their education. . . . Shall we send our men into battle with Civil War muskets if the supply of modern arms is deficient? Of course not. Anybody can see how ridiculous and murderous that would be. But perhaps only doctors themselves can appreciate how murderous a half-baked medical officer can be.

Is it necessary that this large number of medical officers be provided? If it is then everybody will be glad to make the best of it. The armies of other countries have not been furnished with anything like so high a proportion of medical officers. The British, the Australian, and the Canadian armies, for example, get along with a proportion only a little more than half of what is felt necessary by our armed forces; and the quality of the work done is excellent. . . . Is not this demand for so many medical officers an unjustifiable extravagance for which there is no demonstrated need?

These remarks have been directed at the evil effects upon the medical officers themselves caused by the disruption of the only plan for developing properly trained surgeons which has ever been found to work. A similar editorial could be written on the disaster to the civilian population. Are we to go backward a quarter of a century and to surrender to our two great allies the enviable position in medicine which this country occupied before the war? The British Commonwealth and Russia have not found it necessary to disrupt their medical education to anything like the extent which we have been forced to do. As a result we may find ourselves a poor third in medicine in the postwar world. Is it necessary? I know of no convincing evidence that it is. But nothing will be done to remedy the situation unless the medical profession itself, the only body capable of understanding how a medical officer should be educated, speaks its mind loud enough for Congress and the President to hear. Reduce the 6.5 ratio to a reasonable one and much of the basis for the wrecking of our medical education will disappear. The 9-9-9 plan will not train surgeons and will not provide competent surgical officers. Still less will the nine months' rotating internship. That plan should be scrapped and in its place a reasonable program for the training of medical officers should be substituted immediately after a proper inventory of the real needs of the armed services has been made. . . .

Dr. Graham's plea for "a reasonable program for the education of medical officers . . . after a proper inventory of the real needs of the armed

forces" seems justified, and it is likely that this would result in the correction of the other faults. As he suggests, and as Dr. Loyal Davis claims in an editorial published in the September issue of *Surgery, Gynecology and Obstetrics*, the chief source of trouble, at least so far as the Army is concerned, stems from the fact that the Medical Department, a relatively independent unit prior to February, 1918, is part of the Army Service Forces; the Surgeon General and the medical officers in combat zones are under the control of the General Staff, which includes no medical officer, with the result that all matters of policy must be approved or presented for higher consideration by line officers. Due credit should be given to the Directing Board of the Procurement and Assignment Service for being able to maintain the minimum required medical personnel on the home front, thus giving to the Army every physician who could be spared; on the other hand, this board's power is limited, and proper co-operation can be hoped for only if the Medical Department is completely reorganized. The Surgeon General of the Navy is not handicapped by such limitations, and as Dr. Davis points out, the Surgeon General of the Russian Army is directly responsible only to the Chief of Staff. A similar arrangement should obtain in the Army of the United States, and the medical profession should so inform their representatives in Washington, with the hope that the latter will act with courage and force.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

HALTON — Edward P. Halton, M.D., of Holyoke, died October 18. He was in his sixty-third year.

Dr. Halton received his degree from Yale University School of Medicine, New Haven, in 1905. He was a member of the American Medical Association.

His widow, two sons and a sister survive.

NOTICES

AMERICAN FEDERATION FOR CLINICAL RESEARCH

An all-day meeting of the Eastern Section of the American Federation for Clinical Research is being planned for December 9. Investigators desiring to read papers on clinical research should submit an abstract of not over 200 words to Dr. Orville Bailey, Harvard Medical School, 25 Shattuck Street, Boston 15, before November 15. The meeting will be held in Boston and will be open to members of the medical profession.

BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held in the Main Lecture Room of the Harvard Biological Laboratories on Wednesday, November 15, at 8 p.m.

PROGRAM

Milkman's Disease. Dr. F. Albright.

On the Enzymatic Splitting of Lecithin in Animal Organisms. Drs. G. Schmidt and S. J. Thannhauser.

Werner's Syndrome (Progeria of the Adult) and Rothmund's Syndrome. Dr. S. J. Thannhauser.

FORUM ON ALLERGY

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HODGKIN'S DISEASE*

III. Symptoms and Course

HENRY JACKSON, JR., M.D.,† AND FREDERIC PARKER, JR., M.D.‡

BOSTON

IN THE present installment of this series of papers on Hodgkin's disease, the initial symptoms of the three types of that condition will be discussed, and the general course of the disease will be briefly illustrated. In a subsequent issue, the symptoms and signs arising from involvement of certain organs will be discussed in more detail.

Hodgkin's Paragranuloma

Hodgkin's paragranuloma is a comparatively benign condition the onset of which is virtually always heralded solely by painless lymphadenopathy, usually in the cervical region (Table 1).

Systemic symptoms are absent at first, and the patient appears to be in good health. Occasionally the disease is discovered on routine physical examination.

According to our experience, approximately 20 per cent of the cases progress after months or years to Hodgkin's granuloma. It must be em-

TABLE 1. Initial Symptoms of Hodgkin's Paragranuloma (28 cases).

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The course of Hodgkin's paragranuloma is extremely variable. In certain cases, there develop

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signs or symptoms suggesting a transition to Hodgkin's granuloma and death ensues within a short time; in others, many months or several years elapse before the development of Hodgkin's granuloma; in still others, the condition remains quiescent for many years, and death may be due to some intercurrent disease or the patient may survive and remain in excellent health for many years. In these last cases, however, there is always the possibility that the disease will once more become active or that Hodgkin's granuloma will develop. This has been seen to happen as long as nineteen years after the initial lesion was discovered. Involvement of the mediastinal lymph nodes may take place; this does not necessarily imply that Hodgkin's granuloma is developing, but enlargement of the spleen has, in our experience, been an ominous sign. The onset of systemic symptoms, such as fever, weakness, anorexia or loss of weight almost always indicates that a transition to the granulomatous form has taken place. There is no characteristic blood picture, although one occasionally finds an increased percentage of polymorphonuclear neutrophils. There is no anemia.

The following case histories illustrate the course of the disease.

CASE 1. J. H. (Pv. 5-42), a 40-year-old man, was first seen on May 20, 1942. Six years previously, he had noted a lump in the left groin. This did not bother him, and it remained approximately the same size until September, 1941, when it began to increase in size. It was therefore removed, and showed the typical features of Hodgkin's paragranuloma. There was also a small lymph node in the right axilla. Otherwise the physical examination was within normal limits. The blood picture was normal. A moderate amount of x-ray therapy was given to the left groin and to the node in the axilla.

The patient remained well until September, 1942, when he noticed some pain in the right upper quadrant of the abdomen and increasing weakness necessitating his resting when he returned home from work. At that time, there were a few small lymph nodes in both sides of the neck and in each groin. The spleen was palpable 4 cm. below the costal margin. Otherwise the physical examination revealed no notable abnormalities. The red-cell count was normal, but the white-cell count had risen to 20,000, with 80 per cent polymorphonuclear neutrophils. A moderate amount of x-ray therapy was given to each quadrant of the abdomen,

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and any system may appear to be primarily implicated.

Initial Symptoms

As will be seen from Table 2, painless enlargement of cervical lymph nodes is by far the most frequent initial symptom of the disease. They may be situated in the anterior or posterior triangles or under the sternomastoid muscle. Not infrequently an upper respiratory infection has immediately preceded the enlargement, which may

TABLE 2. Initial Symptoms of Hodgkin's Granuloma (213 cases).

SYMPTOMS	NO. OF CASES
Enlarged cervical lymph nodes	111
Pain (usually in abdomen or back)	26
Weakness	14
Enlarged axillary lymph nodes	14
Enlarged inguinal lymph nodes, anorexia, cough	9 each
Dyspnea, loss of weight, abdominal mass	7 each
Chills	5
Itching	4
Vomiting	3
Weakness of legs, amenorrhea, fever, hematemesis, edema of legs, hemoptysis	2 each
Melenia, sternal mass, dysuria, enlargement of tonsil, sore throat, skin nodules, constipation, deafness, dysphagia, cyanosis, sweats	1 each

diminish greatly with the subsequent subsidence of the acute process, so that the physician is not unnaturally led to suppose that he is dealing with a simple inflammatory lymphadenopathy and treats the case accordingly. In other cases, a varying though moderate degree of lymphadenopathy is present over a considerable period of time, and increases after a respiratory infection to such a degree as to demand medical attention. This sequence of events is seen in the following case.

CASE 5. R. E. S. (P. H. 13671), a 24-year-old woman, was admitted to the hospital on March 10, 1938. In the spring of 1933, she had noticed enlarged, painless, nontender lymph nodes in the left side of the neck. There was no associated sore throat or upper respiratory infection, nor were there any constitutional symptoms. For the next 5 years, the nodes fluctuated in size for no ascertainable reason, varying from 1 to 2 cm. in diameter. Occasionally they disappeared entirely. There were no constitutional symptoms. In January, 1938, the patient developed an acute upper respiratory infection of considerable severity, and immediately thereafter the cervical nodes increased rapidly in size.

On entry to the hospital, physical examination revealed an obese, healthy-looking woman. In the anterior and posterior triangles of the left side of the neck and beneath the sternomastoid muscle were several firm, nontender lymph nodes varying from 2 to 5 cm. in diameter. There was no other lymphadenopathy, but the upper part of the mediastinal shadow was definitely widened in the x-ray film. Aside from a moderate elevation of the white-cell count and an increase of the percentage of polymorphonuclear neutrophils in the peripheral blood, the laboratory findings were within normal limits. A biopsy of one of the cervical lymph nodes showed Hodgkin's granuloma. Appropriate x-ray therapy was directed to the neck and mediastinum, with complete disappearance of all masses. The patient was still in excellent condition and gaining weight when last seen in May, 1944.

In a adult, the persistence of notably enlarged lymph nodes for a considerable period of time after an acute upper respiratory infection or the development of persistent masses in the neck after minor

infections must be regarded with suspicion, particularly if the posterior triangle or the supraclavicular region is involved. Painless enlargement of lymph nodes in the neck unassociated with obvious infection always calls for careful investigation, and it has been our experience that without biopsy an accurate and definitive diagnosis cannot be made.

The enlarged lymph nodes are usually nontender, and rarely cause pain unless they press on adjacent nerves or are adjacent to obvious septic foci. Later, pain due to lymphadenopathy is more frequent, particularly when the lymph nodes are in the groin or the axilla. The overlying skin is usually normal in appearance, and the nodes are seldom fixed to the surrounding structures, although they may become immobile by the very fact that they fill the entire neck and impinge on contiguous fixed structures. It should be borne in mind, however, that as a result of poulticing or other self-medication, the overlying skin may become reddened and that an associated infection in the nasopharynx may cause the nodes to be temporarily painful and tender, even in the early stages of the disease. In consistence, the nodes are usually firm and rubbery, occasionally soft and rarely hard. They never have the stony feel so suggestive of metastatic carcinoma, unless they have already been subjected to heavy radiation. On rare occasions, the nodes are extremely soft and even fluctuant.

In our experience, there is no predilection for one or another side of the neck, and in the majority of cases, the involvement is bilateral when the patient is first seen, although almost invariably one side is involved to a far greater extent than the other, and only rarely does one see the evenly distributed bilateral nodes of uniform size and relatively soft consistence so often found in lymphatic leukemia. No particular part of the cervical region appears to be most frequently involved. It is wise, however, to search with special care for nodes beneath the sternomastoid muscles and in the region immediately above the clavicles. Enlarged nodes are not infrequently found in the submaxillary and submental regions, but those confined sharply to such regions are rarely due to Hodgkin's granuloma and are likelier to be secondary to some obscure infection of the floor of the mouth. This fact may be of some practical value in diagnosis.

Enlarged lymph nodes elsewhere, as in the axilla, groin and inguinal regions, have in general the same characteristics as those in the neck, although they are more prone to be painful and only rarely fluctuate in size, probably owing to the fact that they are less likely to be influenced by adjacent infectious processes.

Pain is the next most frequent initial complaint, but it should be emphasized that early in the course of Hodgkin's granuloma this symptom is compar-

and the patient improved considerably and gained weight. Nevertheless, a month later he again began to feel poorly and noted an elevation of temperature each afternoon. He was readmitted to the hospital and was found to have generalized lymphadenopathy. The red-cell count had fallen to 3,900,000, and he was therefore given several transfusions of whole blood. The x-ray examination of the chest showed numerous small patches of consolidation the nature of which was somewhat uncertain, although it was believed that since several of them were definitely nodular, the lesions probably represented metastases from a newly developed Hodgkin's granuloma. This suspicion seemed to be substantiated by the fact that the pulmonary lesions cleared up after an x-ray dosage of 1600 r had been given to the chest. X-ray therapy was then directed to the peripheral lymph nodes. The patient's general condition, however, did not improve. The fever continued, and he began to have drenching night sweats.

In January, 1943, generalized lymphadenopathy appeared. The red-cell count gradually fell to 1,600,000 and the hemoglobin to 35 per cent. Following further x-ray therapy and several blood transfusions, the patient improved somewhat and the fever subsided. After a very short time, however, the weakness and fever returned and the patient grew steadily worse until his death on March 20, 1943.

Autopsy showed widespread involvement by typical Hodgkin's granuloma.

This case illustrates the rapidity with which Hodgkin's paraganuloma occasionally develops into Hodgkin's granuloma.

CASE 2. F. S. (Pv. 8-29), a 45-year-old man, in 1927 first noticed a few small, painless lymph nodes beneath the right sternomastoid muscle. In 1929, a node was removed that on subsequent review showed the typical picture of Hodgkin's paraganuloma. There were no general symptoms at that time, the patient felt perfectly well, and no other abnormalities were noted on physical examination. X-ray treatment was given to the right cervical area, and the patient remained entirely asymptomatic for 6 years, — March, 1935, — when enlarged lymph nodes were noted in the left side of the neck. These were excised and showed a histologic picture suggesting a transition between Hodgkin's paraganuloma and Hodgkin's granuloma. X-ray therapy was again given, the lymph nodes subsided, and the patient remained asymptomatic until March, 1938. At that time, he developed a moderate degree of anorexia and definite bitemporal hemianopsia. He became weak, listless and apathetic. Physical examination was essentially normal except that the visual fields were notably contracted and the spleen could be felt 3 cm. below the costal margin. He was given an x-ray dosage of 600 r at 250 kv. to each side of the head, and his symptoms entirely subsided.

In June, 1938, the anorexia returned. In addition, the patient, a highly intelligent man of robust stature, noticed that all food tasted unusually sweet. With the passage of time, this sense of sweetness became so great that the patient, although co-operative, was unable to eat anything except the most highly spiced foods, and but little of these. A large mediastinal mass was visualized by x-ray, and a moderate degree of hypochromic anemia had developed. The white-cell count, normal at all previous examinations, had risen to 17,000, with 85 per cent polymorphonuclear neutrophils. The patient was given an x-ray dosage of 1000 r at 100 kv. to the head, with some temporary relief from the sensation of sweetness. The mediastinal mass completely disappeared after 800 r to the anterior part of the chest. The anorexia, however, became increasingly severe, and for the next 6 months the patient subsisted almost entirely on peptonized milk and hard-boiled eggs, to each of which he added, in order that they might not "taste too sweet," astounding amounts of cayenne pepper. There was no suggestion of hysteria, and all those who examined him were convinced that the symptoms had an organic basis, although no one was able to localize the lesion. He became extremely emaciated, as might well be expected, and died on April 27, 1939, 10 years after the onset of his condition.

Autopsy failed to reveal, even after the most careful and scrupulous examination, any lesion, either gross or microscopic, in the nervous system to account for the hemianopsia or the abnormality of taste. A few enlarged lymph nodes,

particularly about the head of the pancreas and in the retroperitoneal area, showed the histologic changes of Hodgkin's granuloma. The most prominent lesion seen was an extreme degree of amyloidosis, chiefly in the lymph nodes, kidneys, liver and spleen. Although Hodgkin's granuloma was found at autopsy, the lesions were not extensive enough to cause death, which must be attributed to inanition following extreme anorexia, the cause of which remains entirely obscure.

CASE 3. J. H. (B. C. H. 408240), a 17-year-old man, was admitted to the hospital on September 22, 1920, with the sole complaint of painless lymph nodes in the right side of the neck. The past history had been uneventful. In 1915, he noted a few small lymph nodes in the right side of the neck. These increased slowly in size, and in 1917 one was removed for diagnosis. No record of this biopsy had been preserved. In August, 1920, the patient complained of an increasing sense of constriction in the neck and upper thorax and noticed that the lymph nodes in the cervical region had increased greatly in size.

Physical examination at that time revealed no abnormalities except for the presence of a large number of firm, elastic nodes in the right side of the neck, extending from the mastoid region to the supraclavicular area. A radical dissection was done and all the apparently diseased tissue was removed. Examination of the lymph nodes showed the typical picture of what we now recognize as Hodgkin's paraganuloma. Unfortunately, the patient was told by one of his friends that he would die in 6 months, and as a respite from this gloomy outlook, he had recourse to hard liquor in large amounts. At the end of a year, he was still alive but was unable to forego alcohol. He remained symptom-free, however, until September, 1939, when he again noticed nodes above the clavicle and a sense of tightness in the neck. Physical examination showed many firm nodes above the right clavicle; these appeared to extend into the thoracic cage. A biopsy showed that the process had progressed into a typical Hodgkin's granuloma. A large mediastinal mass developed, and in spite of x-ray therapy, the patient died in 1942, 27 years after the initial lymphadenopathy and 3 years after the known transition of the Hodgkin's paraganuloma into Hodgkin's granuloma.

CASE 4. L. C. (Pv. 2-36), a 36-year-old woman, was admitted to the hospital in April, 1936. In 1910, at the age of 10 years, enlarged lymph nodes had appeared in the right side of the neck. These had been removed at another hospital and showed the histologic picture of what we now call Hodgkin's paraganuloma. The patient remained entirely well until 1917, when the nodes recurred. They were removed and again showed precisely the same features as they had in 1910.

No further signs or symptoms occurred until February, 1936, when masses were once more noted in the right side of the neck. Physical examination showed no abnormalities except that beneath the upper third of the right sternomastoid muscle were a group of firm, freely movable nodes. These were excised as completely as possible, and they too showed the histologic features of Hodgkin's paraganuloma. Thus there had been no appreciable change in the histologic picture since 1910. At present, 34 years after the initial lymphadenopathy, the patient is free of signs and symptoms.

This case illustrates the benign character of the process when it remains unaltered. Why one patient rapidly develops Hodgkin's granuloma whereas another remains in comparatively good health is entirely obscure.

HODGKIN'S GRANULOMA

It is of the greatest importance to recognize clearly the extraordinarily protean character of the symptomatology of Hodgkin's granuloma. It is true that in the majority of cases painless enlargement of one or more cervical lymph nodes first attracts the patient's attention to his condition, yet so diverse are the symptoms and so varied are the signs that almost any disease may be simulated

General Course

In the great majority of cases, Hodgkin's granuloma progresses inexorably to a fatal termination, but the course is extremely variable, and aside from the broadest generalities, it is impossible in any given case to predict what changes will take place or precisely when they will occur. Virtually any organ or tissue in the body may be involved, and the clinical course of the disease depends in large measure on the extent and rapidity of the spread as well as on which organs are involved. In one case, the pathologic changes may become so widespread and so all-inclusive that no organ can properly fulfill its function, and death ensues from a sort of general attrition; in another, sudden death may occur at a time when the patient seems to be in comparatively good health.

The disease does not advance in an even, orderly fashion. Remissions occasionally occur in a quite unpredictable manner, and patients who have seemed to be failing under the best of treatment may unaccountably respond most favorably to what is regarded as a final therapeutic gesture. On the other hand, it is not unusual to see a patient who has been doing especially well for many months or even years become rapidly worse and die within a few weeks.

In view of these facts, it seems profitless to attempt any working classification of the various clinical types that are met with in practice. It is true that in one case, the process may be confined largely to the mediastinum, in another to the spleen and in still another to the gastrointestinal tract. In some cases anemia is a marked feature, in others high fever. A patient may be seen in whom loss of weight and strength has been, from the onset, a striking feature; again, a patient may be able to continue hard physical labor until the end is but a short way off. In this sense, there are clinical types, yet each case is a law unto itself, and the disease can be treated more intelligently if this fact is constantly borne in mind.

Hodgkin's granuloma only rarely progresses sharply into Hodgkin's sarcoma, a far more malignant form of the disease. Such transformation is far less frequent than the comparable progression of Hodgkin's paraganuloma into Hodgkin's granuloma.

The following cases illustrate the varied course of Hodgkin's granuloma.

CASE 8. C. C. (C. H. 167400), a 6-year-old girl, was admitted to the hospital on January 1, 1933. The past history was irrelevant. She had always seemed healthy. Approximately 3 weeks before entry, the parents had noticed enlarged lymph nodes in each side of her neck. These increased rapidly in size, and a week later she developed a severe cough, associated with some hoarseness and a moderate elevation of temperature. For a week before entry, she had had marked anorexia.

Physical examination on admission revealed a well-developed and well-nourished girl suffering from a marked degree of dyspnea. In the anterior posterior triangle of both sides of the neck were numerous rubbery lymph nodes

1 to 4 cm. in diameter. They were not attached to the skin or to the underlying tissues. The throat appeared normal. Examination otherwise revealed nothing abnormal except for a pronounced widening of the mediastinal dullness, a finding that was confirmed by x-ray examination. The temperature was 102°F., the pulse 140, and the respirations 30. The red-cell count was 3,800,000 and the white-cell count 13,400, with 72 per cent polymorphonuclear neutrophils, 2 per cent myelocytes, 20 per cent lymphocytes and 6 per cent monocytes. A biopsy of one of the cervical lymph nodes showed the picture of Hodgkin's granuloma. The patient's dyspnea increased, the temperature rose to 104°F., and she died of respiratory failure less than a month from the apparent onset of her condition.

CASE 9. K. A. D. (H.H.36-542), a 20-year-old man, was admitted to the hospital on May 25, 1936. A year before entry, he had had a mild upper respiratory infection, following which there had appeared an enlarged lymph node in the right side of the neck. There was no impairment of general health. The node was neither tender nor painful, but it persisted after the subsidence of the respiratory infection. Eight months later, the patient's family noticed that he was becoming pale. For several weeks before admission, he ran a septic type of temperature and had many drenching night sweats. Shortly thereafter, there appeared edema of the ankles and scrotum, and coincidentally both the hearing and vision began to fail.

Physical examination on entry showed an emaciated man lying apathetically in bed. His vision was markedly impaired, and he could not read the largest newspaper type. The left eye showed a moderate degree of enophthalmos and was deviated downward and inward. The right fundus oculi showed several patches of exudate similar to that seen in chronic nephritis, and in addition a large area of chorioretinitis on the temporal side of the disk. In neither ear could the patient hear the tick of a watch. Both nostrils were filled with clotted blood, and the lips were parched, cracked and bleeding. In the right side of the neck from the angle of the jaw to the supraclavicular space were many firm, discrete lymph nodes averaging 2 cm. in diameter. Recently there had been excised from this region a lymph node showing the typical picture of Hodgkin's granuloma. In each groin were large numbers of firm, tender lymph nodes, and many similar ones could be felt deep in the pelvis above the pelvic brim. The heart was normal in size. Signs of moderate ascites were present, but neither the liver nor the spleen could be felt. There was marked edema of both legs and of the scrotum and penis. The red-cell count was 2,130,000, the hemoglobin 50 per cent (Sahli), and the white-cell count 2000, with a normal differential count. The platelets were greatly diminished. The urine contained a slight trace of albumin and a few red cells. The temperature was 103°F., and the pulse 130.

Since the disease was obviously widespread, involving the central nervous system, ears, eyes, chest, abdomen, pelvis, bone marrow and peripheral lymph nodes and since his condition seemed desperate, it was decided to give several blood transfusions before instituting x-ray therapy. In addition, he was put on a high-caloric diet.

Between May 26 and June 11, three blood transfusions totaling 1600 cc. were given, with the result that the hemoglobin rose to 50 per cent and the red-cell count to 3,500,000. During the interval, his general condition remained essentially unaltered but, interestingly enough, the hearing improved sufficiently so that the patient could hear a watch tick in both ears and could understand normal conversation. The eyesight also improved, although not to the same extent. The patient's condition appeared to warrant the institution of x-ray therapy, and inasmuch as the most marked lymph-node involvement was in the pelvis, radiation was directed to that area, and from June 11 to 15 he received 275 r of high-voltage x-rays. He suffered no untoward reaction to this small amount of radiation, so that between June 15 and 22 he was given 1000 r to the abdomen. The temperature remained elevated, the physical examination was essentially unaltered, and the general condition seemed, if anything, rather worse. The patient became jaundiced and even during the day was somewhat drowsy. He took no notice of his surroundings, and it was difficult to arouse him from his almost constant lethargy. The red-cell count had fallen to 1,940,000 and the hemoglobin to 32 per cent.

The outlook was certainly not bright, and all therapeutic measures to date appeared to have been unavailing. In view

atively rare. In Hodgkin's sarcoma and reticulum-cell sarcoma, on the other hand, pain is often an early and almost constantly a late symptom. The most frequent sites of pain are the abdomen and the back. In the former, it is in most cases caused by retroperitoneal lymph nodes, and it is perhaps surprising that this symptom is not found oftener, for many authors have emphasized the frequency with which the retroperitoneal nodes are involved, and our own experience is in agreement with this finding.

Only rarely is pain due to invasion of one of the abdominal viscera as in the following case.

CASE 6. E. M. (B. C. H. 559573), a 47-year-old man, was admitted to the hospital on May 10, 1923, with a chief complaint of upper abdominal pain. Thirteen years previously, he had been operated on for a "perforated gastric ulcer." No data were available as to the nature of this ulcer. Convalescence, however, had been uneventful, and the patient remained symptom-free until January, 1923, at which time he began to suffer from a burning epigastric pain occurring shortly after meals and lasting approximately an hour. There was no nausea or vomiting. During the next 3 months, he lost about 15 pounds, and 3 days before entry to the hospital he vomited "a cupful" of bright-red blood.

Physical examination on admission showed evidence of an old healed tuberculous process in the apex of the right lung and a moderate degree of anemia. The abdomen showed no tenderness, spasm or masses. X-ray examination revealed an extensive irregularity and mottling of the cardia and media of the stomach, and a diagnosis of carcinoma was made. The red-cell count was 3,280,000, the hemoglobin 55 per cent (Sahli) and the white-cell count 16,000, with 86 per cent polymorphonuclear neutrophils, 10 per cent lymphocytes and 4 per cent monocytes. The stools gave a strongly positive guaiac test. The patient failed rapidly, and in spite of two blood transfusions, the red-cell count fell to 2,800,000 and the hemoglobin to 40 per cent. Persistent vomiting developed, and he died 3 weeks after entry.

Autopsy showed extensive Hodgkin's granuloma of the stomach, with extension into the liver and pancreas and involvement of the gastric and retroperitoneal lymph nodes.

Rarely abdominal pain is caused by great enlargement of the spleen.

Pain in the back, usually in the lower thoracic or lumbar region, may be due to a variety of causes. In obscure cases, one is often forced to the conclusion that enlarged lymph nodes are pressing on one or more spinal nerves. Not infrequently back pain is due to direct involvement of the bodies of the vertebrae or to granulomatous lesions in the dura or epidural space, and it is of the greatest importance to recognize the fact that lesions of the spine may be present for several months before they can be visualized on x-ray films. Pain due to involvement of bone is well illustrated by the following case.

CASE 7. B. B. (H. H. 36-543), a 34-year-old woman, was admitted to the hospital on May 25, 1936. In February, 1933, she began to complain of fleeting pains of no great severity in the low lumbar region. The pain was made worse by exercise, and was not constant. A careful physical examination at that time by her physician revealed only slight tenderness and spasm of the muscles in the right lumbosacral region. The symptoms continued with exacerbations and remissions, in spite of baking, massage and simple orthopedic measures, until May, 1935. The pain then became constant, was much worse at night and radiated from the lumbar region bilaterally to the lower abdomen. Nine months later,

in February, 1936, the patient began to lose weight and to complain of anorexia, nausea and occasional attacks of vomiting.

Except for evident loss of weight, — she had lost 25 pounds, — the physical examination showed only a few discrete, firm, bean-sized lymph nodes in each side of the neck. The red-cell count was 3,890,000, the hemoglobin 63 per cent (Sahli), and the white-cell count 33,000, with 90 per cent polymorphonuclear neutrophils and 10 per cent lymphocytes. X-ray films of the spine and pelvis showed extensive hyperplastic changes in the bodies of the 3rd, 4th and 5th lumbar vertebrae and in the left portion of the pelvis consistent with those of Hodgkin's granuloma. A biopsy of a small node in the right side of the neck showed the typical picture of that condition. X-ray therapy relieved the back pain for a few months, but splenomegaly, hepatomegaly and a left-sided pleural effusion developed, and the patient died in early October, 1937, 19 months after the bone lesion had been demonstrated by x-ray.

When the change from Hodgkin's paraganuloma to Hodgkin's granuloma actually first developed is of course, problematical, but this case illustrates the importance of careful x-ray studies in patients with obscure and recalcitrant back pain, and the wisdom of searching for enlarged lymph nodes that may give a clue as to the true condition.

Pain in the chest, shoulder, groin, leg or axilla is occasionally encountered as an initial symptom. Usually under such circumstances unequivocal evidence of Hodgkin's granuloma is present.

Generalized weakness is not infrequently the first symptom, and in the absence of obvious lymphadenopathy or splenomegaly may be a most difficult one to evaluate. A careful search should be made for enlarged lymph nodes and abdominal masses, and the finding of an elevated basal metabolic rate or an elevated white-cell count with an increased percentage of polymorphonuclear neutrophils may be of some diagnostic significance.

Not infrequently, symptoms referable to the gastrointestinal tract first attract the patient's attention. If there has been melena or hematemesis, some intrinsic lesion is usually discovered at autopsy. Other symptoms, such as anorexia and nausea, can only rarely be traced to such an intrinsic lesion.

Finally, there are a considerable number of the most varied initial signs and symptoms, such as anorexia, edema of the legs, dyspnea, loss of weight, abdominal masses, cough, generalized itching, amenorrhea, hemoptysis, persistent sore throat, vomiting, hematemesis, dysphagia, melena and deafness. One can only bear in mind that Hodgkin's granuloma may first manifest itself in such ways and endeavor to prove whether it is present.

In a considerable number of cases there is initially a combination of several symptoms, in which event the condition is usually already well advanced. Yet it should be pointed out that this fact by no means necessarily militates against relatively successful therapy.

It is thus clear that Hodgkin's granuloma is usually first manifest by painless cervical lymphadenopathy, but that its initial stage may be marked by the most diverse symptoms and signs.

symptom, but the enlarged lymph nodes seldom atrophy in size as they frequently do in Hodgkin's granuloma. Weakness, dyspnea, cough and vomiting may be seen early. Rapid loss of weight is much more frequent than in Hodgkin's granuloma and may be the outstanding feature of the disease. Thus, pain was an initial complaint in over 50 per cent of our cases of Hodgkin's sarcoma, whereas it was present initially in only 12 per cent of patients suffering from Hodgkin's granuloma. Symptoms suggesting involvement of internal organs were noted at onset in 75 per cent, whereas they were present in less than 30 per cent of the patients suffering from Hodgkin's granuloma.

On the average, patients sought medical advice within five months of the apparent onset of their disease, yet even after this short interval the initial complaints had been almost invariably supplemented by many others, and during the course of the disease, still further symptoms reflect the rapidly

TABLE 4. *Symptoms During Course of Hodgkin's Sarcoma (32 cases).*

SYMPTOMS	NO OF CASES
Fatigue	28
Loss of weight	26
Pain	21
Dyspnea	16
Anorexia	14
Cough	14
Edema	13
Fever	8
Constipation	7
Vomiting	7
Epistaxis	4
Hematuria	3
Jaundice	3
Night sweats	3
Chills	3

invasive and malignant character of the tumor. The disease runs an insidiously rapid course even though the initial response to x-ray therapy may have appeared to be good. Fatigue and rapid loss of weight are frequent. The majority of patients develop pain referable to the organs or tissues involved, and often there is cough due to the frequent involvement of the lung. Fever, on the other hand, is rare; by contrast its frequency in Hodgkin's granuloma is well known. Symptoms and signs referable to the various organs will be discussed in more detail in a subsequent paper. In general, it may be said that Hodgkin's sarcoma runs the course of a highly malignant neoplasm.

The following cases illustrate the course of the disease.

CASE 13. G. P. (B. C. H. 92408), a 37-year-old man, entered the hospital in October, 1929, because he had had epigastric distress for the previous 2 months. The pain was constant, radiated to the umbilicus and was greatly aggravated by the ingestion of food. There had been no vomiting, hematemesis, melena or jaundice. There were no other symptoms of importance, and the past history was irrelevant.

On physical examination, a freely movable mass the size of an orange was felt in the epigastrium. In each axilla and in each side of the neck were several firm lymph nodes 4 to 5 cm. in diameter. The spleen was felt 3 cm. below the costal margin. There were no other abnormalities of note. The temperature was normal. The red-cell count was 4,000,000,

the hemoglobin 92 per cent (Sahli), and the white-cell count 25,000, with 75 per cent polymorphonuclear neutrophils, 23 per cent lymphocytes and 2 per cent monocytes. Biopsy of one of the axillary lymph nodes showed Hodgkin's sarcoma.

Six hundred roentgens of x-ray therapy was given to the abdomen and to the nodes in the axilla and neck. Two weeks later, neither the epigastric mass nor the superficial lymph nodes could be felt. The response to radiation was dramatically satisfactory, and for 6 months the patient felt perfectly well. In April, 1930, however, he returned to the clinic and enlarged lymph nodes were found in the cervical, axillary, inguinal and popliteal regions. No abdominal mass could be felt. Six hundred roentgens of x-ray therapy were given to each involved area, but there was little if any subsequent improvement in the patient's condition, in spite of this dosage and subsequent additional x-ray therapy. Indeed, he soon began to complain once more of severe epigastric pain, especially after meals, and of vomiting, weakness and marked loss of weight.

In August, 1930, the patient was readmitted. At that time, there were in each side of the neck and in each axilla firm lymph nodes 10 cm. in diameter that were neither fixed nor tender. The spleen was found to be 5 cm. below the costal margin, and the liver was barely palpable on deep inspiration. The red-cell count had fallen to 1,230,000 and the hemoglobin to 35 per cent (Sahli). The white-cell count was 2550, with 90 per cent polymorphonuclear neutrophils, 8 per cent monocytes and 1 per cent lymphocytes. The urine examination was negative.

From then until his death 3 weeks later, the patient ran an irregular fever to 100°F. and the pulse gradually rose from 90 to 130. The right leg became edematous, presumably from pressure of lymph nodes in the inguinal region, and in the right parietal bone of the skull there developed a palpable defect. X-ray examination showed a large erosion of the skull in this region. Many petechiae appeared in the skin of the chest and abdomen and in the mucous membranes of the mouth. The patient failed steadily and died on August 20, 1930, just a year after the appearance of his first symptom.

Autopsy showed Hodgkin's sarcoma involving the retroperitoneal, mesenteric, mediastinal, cervical, axillary and inguinal lymph nodes, as well as the spleen, liver, kidneys, pancreas, adrenal glands, duodenum, ileum, colon, lumbar vertebrae and skull.

CASE 14. P. C. (H. H. 24-806), a 49-year-old man, was first seen in June, 1924, at which time he complained of pain in the throat. Two and a half months before entry, he had had frequent sore throats. Otherwise, the history was noncontributory.

On examination, the right tonsillar fossa was found to be occupied by an ulcerated tumor 6 cm. in diameter. It was not bleeding. A moderately large, firm lymph node was palpable beneath the angle of the right mandible. No other abnormalities were noted on physical examination. The patient was instructed to return 1 week later for biopsy and further study, but he did not reappear until September, 3 months afterward. In the interim, his sore throat had recurred at irregular intervals without any specific treatment. Examination showed in the right tonsillar region a tumor that extended high up into the nasopharynx. No lymph nodes were felt in the neck. There were no other abnormalities. The red-cell count was 5,800,000, the hemoglobin 95 per cent (Sahli), and the white-cell count 5600 with 55 per cent polymorphonuclear neutrophils, 37 per cent lymphocytes, 5 per cent eosinophils and 3 per cent monocytes. A biopsy was performed, and the lymph node removed showed all the characteristics of what we now call Hodgkin's sarcoma.

In November, 1924, eight radium seeds of 1 m.c. each were implanted in the tumor, and within 6 weeks it had completely disappeared. The patient remained asymptomatic for 6 months.

In June, 1925, he again developed a sore throat, and the left tonsil was found to be enlarged and ulcerated. Implantation of radium seeds (four of 1.5 m.c. each and two of 1 m.c. each) resulted in rapid shrinkage in the size of the tumor. In September of the same year, a mass of lymph nodes was palpable in the left side of the neck. One so-called "suberythema dose" of high-voltage x-ray was given over this area. For the next 16 months, the patient felt perfectly well and did not report to the follow-up clinic.

of the falling red-cell count, the patient, between July 1 and 10, was given transfusions totaling 3000 cc. of blood, with a resultant rise of the red-cell count to 3,480,000. By that time, the temperature had come down to normal, the hearing was normal, and the eyesight, although still poor, was much improved. The patient was allowed up and around the wards within the limits of his strength. His appetite, which on admission had been practically nil, was now ravenous. His general condition improved daily, and he rapidly gained both strength and weight. The emaciated, apathetic boy first seen became an optimistic young man. The lymph nodes in all areas became much smaller. The ocular manifestations improved, with the exception of the retinal changes, which remained unaltered. The peripheral edema and ascites disappeared. On July 20, the patient was given another blood transfusion of 500 cc., and on July 25 he walked out of the hospital to return to his home.

In August of the same year, the cervical lymph nodes returned and increased rapidly in size, but after administration of 600 r to each side of the neck they completely disappeared, and the patient seemed in excellent condition and was able once more to return to work as a laborer.

He continued to work at hard manual labor until December, 1936, when he again became weak and complained of anorexia, nausea and vomiting and ringing in the ears. There were many firm lymph nodes in each side of the neck. The mediastinal shadow was increased to the right, and the spleen was palpable 3 cm. below the costal margin. The temperature was 103°F., the pulse 130, and the respirations 35. Examination of the blood showed a red-cell count of 1,570,000 and a white-cell count of 4000. The patient was given three blood transfusions of 500 cc. each and 75 r of spray x-ray therapy, both anteriorly and posteriorly. Following this, his general condition improved greatly, the lymph nodes and spleen disappeared, and he was once more able to resume his normal activities. In May, 1937, however, he was again troubled with anorexia and vomiting, and the temperature rose to 102°F. The spleen was barely palpable on inspiration. Many fine rales appeared at the apex of the right lung. There was no return of the lymph-node enlargement, but the patient failed steadily, and again became partially blind and deaf. The temperature remained constantly between 101 and 103°F., the red-cell count fell to 2,630,000, and the patient died on August 25, 1937, which was 2 years and 3 months after the date of his first symptom.

CASE 10. E. M. (P. H. 1887), a 52-year-old man, was in excellent health until May, 1929, when he noticed a small lump in the left axilla. It was neither painful nor tender, and he had no other complaints. Physical examination showed a firm mass 6 cm. in diameter high in the left axilla, a pea-sized lymph node above the left clavicle and a similar one in the left epitrochlear region. Otherwise, the examination showed no abnormalities. The red-cell and white-cell counts were within normal limits, and x-ray films of the chest failed to show any widening of the mediastinal shadow. The axillary and epitrochlear nodes were excised, and each showed the typical histologic picture of Hodgkin's granuloma. The patient was given 900 r to the left axilla and 600 r to the left epitrochlear region.

There have been no recurrences, and the patient has remained well to date, 15 years from his first symptom.

CASE 11. J. P. (P. H. 2757), a 48-year-old, Italian laborer, noted in August, 1930, ease of fatigue, anorexia, night sweats and a mass in the left axilla; he continued at his work, however. Three months later there appeared an enlarged lymph node in the right axilla. This was removed and showed the usual picture of Hodgkin's granuloma. He was admitted to the hospital on December 6, 1930.

Physical examination revealed a firm, nontender lymph node 4 cm. in diameter in the left axilla and several similar ones in the left supraclavicular area. The spleen was palpable 3 cm. below the costal margin. An x-ray film of the chest was normal, and it was specifically noted that there was no evidence of bone involvement. The general condition was good. The red-cell count was 3,850,000, the hemoglobin 60 per cent (Sahli), and the white-cell count 11,400, with 79 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 15 per cent lymphocytes and 5 per cent monocytes. Six hundred r was given to the left side of the neck, with rapid disappearance of the nodes. Three weeks later, however, the patient noticed a raised, tender swelling 6 cm.

in diameter over the lower part of the sternum. X-ray film showed an extensive irregular mottling and destruction of the gladiolus, and on physical examination there was a hard, tender swelling rising 2 cm. above the general level of the sternum and 10 cm. in diameter. The patient was given 600 r to the left side of the neck, each axilla and the spleen at 1000 r over the sternal mass. The nodes disappeared following this treatment. The sternal mass became much smaller but did not disappear.

During the intervening years, he has received 2400 r to the involved area. The last x-ray films still showed the bone destruction, but when last seen in the spring of 1944, 1 years after his first symptoms, the patient was feeling perfectly well and was capable of doing reasonably hard manual labor.

Cases 10 and 11 attest the value of early treatment, and show that Hodgkin's granuloma is not always so rapidly fatal as is generally believed.

CASE 12. A.P. (H. H. 17-646), a 10-year-old boy, in 1911 noticed a plum-sized mass in the right side of the neck. It was excised and showed the histologic features of Hodgkin's granuloma. Physical examination revealed no other abnormalities, and both the past and family histories were noncontributory. The peripheral blood picture was normal. At intervals during the next 8 months, 8200 m. c. h. of radium was given at the site of the lesion and 800 m. c. h. to the mediastinum.

For the next 15 years, the patient remained entirely well except that from time to time minute nodes were noted under the anterior part of the jaw. This minor lymphadenopathy appeared to be due to oral sepsis.

In 1930, at a routine checkup, there was found a mass the size of a small plum in the submaxillary region on the left side. This was removed and again showed the picture of Hodgkin's granuloma. An indeterminate amount of x-ray (probably about 600 r) was directed at the left side of the neck. The patient thereafter remained free of all signs of symptoms up to December, 1941, when he moved to another city and was lost sight of.

Whether this result can properly be regarded as a cure in the true sense of the word is perhaps debatable. That the results were excellent no one can deny, for the patient was alive and well nearly 30 years after the initial lymphadenopathy.

HODGKIN'S SARCOMA

Pain is the most frequent initial symptom of Hodgkin's sarcoma (Table 3). It is most frequent in the abdomen, is usually unrelated to meals,

TABLE 3 Initial Symptoms of Hodgkin's Sarcoma (32 cases)

SYMPTOMS	No. OF CASES
Pain	17
Abdomen	9
Lymph nodes	4
Chest	2
Throat	2
Painless enlargement of lymph nodes	8
Weakness	5
Loss of weight	5
Dyspnea	4
Cough	3
Vomiting	2
Sore throat	2
Anorexia	2

and is occasionally accompanied, even early in the disease, by loss of weight. Pain may, of course, occur elsewhere, and it is to be particularly noted that the superficial lymph nodes are often painful. This is rarely the case in Hodgkin's granuloma. Painless lymphadenopathy may be the sole initial

my or Navy his sex habits have been quite well established, and that regardless of all efforts made in the field of sex education many of these young men will be sexually promiscuous. For such, venereal prophylaxis is advocated. There are those who on moral grounds argue against venereal prophylaxis. Their stand is due in part to the fact that some prophylactics are also contraceptives. There are aspects that a single, simple, clean, nonirritating prophylactic that is not contraceptive but is efficient against both syphilis and gonorrhea will soon be available. If so, it is hoped that much of the present opposition will disappear.

During World War I, the attempt was made to control venereal disease by punitive measures. Men were punished for failing to take a prophylactic after exposure and also for acquiring a venereal disease. Consequently, a soldier's only chance of escaping punishment if he became infected with gonorrhea or syphilis was to conceal his illness. This was frequently done with more or less success by his going to some nonreputable agency for treatment. Often this resulted in his avoiding punishment, but it was notoriously ineffective from the standpoint of curing the infection and protecting public health. Punitive measures have failed in every venereal-disease-control program in which they have been utilized. The modern public-health attitude is to look on gonorrhea and syphilis as communicable diseases and not as crimes, and to consider a venereal infection as a public-health menace until it is brought under control. The most efficient way to get such infections under control is to offer the best possible diagnostic and therapeutic services without the necessity of the patient's losing all his or her self-respect, and to eliminate all punitive measures. The Army has adopted this intelligent attitude. A soldier who now acquires a venereal disease is punished only if he conceals it. He does lose pay for time spent in a hospital for a venereal infection but by authorizing the treatment of gonorrhea on a duty status the Army has made it possible for a man so treated to avoid forfeiture of pay. This is unquestionably good medical and sound public-health practice.

At the beginning of the present emergency, divisions of venereal-disease control were established in the offices of the surgeons general of the Army and Navy. It had long been recognized that if no one is specifically charged with the duty of controlling venereal disease there will be no control, but when certain persons are designated for such a specific duty much progress is made. This has been noted in many of the state health departments, in which during the last several years divisions of venereal-disease control have been established. Both services are to be congratulated for taking such an important step in connection with one of their major problems, and also for their wise selection of officers to head these branches. These well-trained, highly efficient officers are responsible for their respective control programs, which are based on the best scientific

experience so far as it is compatible with the difficulties of military administration. It is obvious that in a theater of operation a venereal-disease-control program must be a compromise between what is the best and what is practicable. It is an old American custom for armchair strategists to point out errors of commission or omission in the conduct of wars. An impartial observer familiar with all the facts could find little if anything to criticize in the way the venereal-disease program is being run in the armed forces, both at home and abroad.

A large group of medical officers who have been given intensive courses of instruction in venereal-disease control are now stationed in the several service commands, naval districts and large military units, where they are functioning as venereal-disease (V.D.) control officers. That the venereal-disease sections are doing an excellent job is revealed by the present situation as contrasted with the past. Turner and Brumfield¹ state that during the last century rates of over 150 per 1000 per annum were not unusual in the Army. The annual rate for 1939 was 29.6 per 1000 per annum, which was the lowest recorded until that time. There are indications that the present rate is even lower. In 1940 the days lost as the result of venereal disease were 1278 per 1000 men, and in 1943 this figure dropped to 400. Although these figures indicate a decided improvement, there were nevertheless 2,824,000 hospital-bed days from January, 1942, to September, 1943, due to venereal disease, which means that there is still too much morbidity.

Every serviceman known to have gonorrhea or syphilis is interviewed by a medical officer who attempts to get from him the identity of his recent sex contacts. The information obtained is sent to the state department of health, whereupon trained epidemiologists attempt to locate the woman and to persuade her to go to some medical agency for an examination. This may be a private physician or a clinic. It is discouraging to note that, of the women who go to a private physician for diagnosis in Massachusetts, infection is detected in 53.2 per cent, whereas 71.6 per cent of those examined in clinics are found to be infected. These figures are statistically significant. It is known that many of the women who go to a private physician and are said to be noninfectious have been and continue to be identified by enlisted men as their only recent sex contacts. This suggests that some physicians are not willing to utilize the most efficient diagnostic procedures available. Some physicians have admitted that laboratory studies were not done because the woman did not have clinical evidence of infection. Experience during recent years indicates that many women found to be infected with gonorrhea do not show any of the so-called "typical" signs or symptoms of the disease.

Cultures, although far from perfect, are more efficient than any other known method in detecting

In February, 1927, he returned complaining of recent difficulty in breathing, severe headache and a painful mass in the neck. The pharynx appeared normal, but there was a bloody discharge from the almost completely obstructed nasal passage and a hard, walnut-sized lymph node was found in the right side of the neck. An x-ray film of the chest disclosed enlarged mediastinal lymph nodes. High-voltage x-ray therapy was given to the thorax and neck, without any beneficial effect. The development of deafness, diplopia, right unilateral exophthalmos and finally blindness bore witness to the rapid extension of the neoplasm within the skull. The patient died on April 22, 1927, just 3 years after the first symptom.

Autopsy showed a tumor having the histologic features of the condition now referred to as Hodgkin's sarcoma, which was primary in the right tonsil. There was direct extension to the nasopharynx, sphenoidal sinus, right orbit, right temporal bone, pituitary gland and dura mater. Metastases were found in the pancreas and mesenteric lymph nodes.

CASE 15. J. C. (B. C. H. 974896), a 53-year-old woman, was admitted to the hospital on February 14, 1940, with the chief complaint of "gas on the stomach." The past history was entirely noncontributory. For 3 weeks prior to admission, she had noted that during or immediately after meals she felt "bloated," and there had been almost constant nausea. Anorexia had been extreme, and she had grown progressively weaker.

Physical examination revealed several enlarged, rubbery lymph nodes behind the left sternomastoid muscle. Otherwise, there were no notable abnormalities. Gastric analysis showed absence of free hydrochloric acid, and both the gastric contents and the stools gave a strongly positive guaiac reaction. The red-cell count was 5,100,000, the hemoglobin 71 per cent (Sahli) and the hematocrit 37. The white-cell count was 4600, with 68 per cent polymorphonuclear neutrophils, 10 per cent lymphocytes, 17 per cent monocytes, 4

per cent eosinophils and 1 per cent basophils. The temperature, pulse and respirations were normal.

A gastrointestinal series showed no abnormality in the esophagus, but x-ray examination of the stomach revealed a large fungating tumor arising near the cardia. The mass appeared to encroach on the esophagus but caused no obstruction. The remainder of the gastrointestinal tract appeared normal.

The patient became increasingly short of breath and failed rapidly. The lymph nodes in the neck increased greatly in size, and within a week there developed signs of obstruction of the superior vena cava. Fluid accumulated in the left pleural cavity, and 2 months after admission 900 cc. of bloody fluid was removed. Anorexia became extreme, and the patient died on April 19, a scant 3 months after the first symptoms.

Autopsy showed extensive involvement of the greater curvature of the stomach by Hodgkin's sarcoma, with direct invasion of the pancreas and diaphragm, massive serous effusion in the left pleural cavity and extensive involvement of the abdominal lymph nodes.

* * *

From the case histories and the discussion above, it should be clear that in broad terms Hodgkin's paraganuloma is a comparatively benign condition occasionally progressing to Hodgkin's granuloma; that Hodgkin's granuloma is characterized by the most protean manifestations, is usually, though by no means invariably, fatal within a few years, and on rare occasions progresses to Hodgkin's sarcoma; and finally that Hodgkin's sarcoma behaves as a highly malignant, comparatively localized tumor rapidly resulting in death.

VENEREAL DISEASE AS A WAR INJURY*

OSCAR F. COX, M.D.†

BROOKLINE, MASSACHUSETTS

VICTORY in the shortest possible time is our objective. It is the duty of every one of us to do all in his power to prevent delay. Morbidity in the armed forces, or among the men and women who produce the munitions without which the fighting men cannot hope to achieve victory, is something that concerns us as physicians. Every case of morbidity among these people is a war injury, and among such cases venereal diseases are high on the list.

During all previous wars in which this country has engaged, the incidence of gonorrhea, and to a lesser extent that of syphilis, has been appalling. The cause of high venereal-disease rates during wartime is largely psychologic. When large numbers of people become affected by war hysteria, a marked increase in sexual promiscuity results. Since promiscuity is the cause of the wide dissemination of the venereal diseases, the less there is in a given group the lower will be the venereal-disease rate. If it were possible to have everyone adhere to the one-man, one-woman ideal, venereal disease would disappear in one generation. Although there appears to be no

hope of attaining such an ideal in the near future, it is a goal toward which society should constantly strive.

Before Pearl Harbor it was my privilege to talk with many high-ranking line officers, most of whom had a sound understanding of sex and venereal disease. An occasional officer, however, expressed himself paradoxically to the effect that a man could not be a good soldier unless he occasionally had sexual relations, but that any soldier so stupid as to acquire a venereal disease was not wanted in his command. As physicians we should like to know what diagnostic procedures the soldier was expected to utilize in order to eliminate the possibility of venereal disease.

Fortunately, the Army and Navy are officially committed to the repression of prostitution. Continence is their number-one approach to the venereal-disease problem. It is the duty of commanding officers to see that all men in their commands are given data about sex and venereal disease, particularly the fact that continence is compatible with manhood and good health. The armed forces are, however, realistic in that they concede that by the time a man is old enough to be inducted into the

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†Associate professor of medicine, Boston University School of Medicine; director, Division of Genitoinfectious Diseases, Massachusetts Memorial Hospitals.

No one yet knows whether penicillin is capable of curing syphilis. Certain facts are known, and these are most encouraging. Mahoney's³ first 4 cases, which were given an eight-day course of treatment, have been observed for eleven months. All became skin-field negative within a few hours after the first injection. This was followed by an early healing of the lesions and a steady drop in the syphilitic reagin titer, and all the serologic tests became negative. One of these patients has yet had a clinical or a serologic relapse. The spinal fluid in each case is negative. Whether or not they have been cured of syphilis will not be known until they have been observed for a considerable period. Since Mahoney's original work many other patients with early syphilis have been treated with penicillin, and although the observation periods have not been sufficiently long to justify final conclusions, their progress to date more or less parallels Mahoney's results.

The modern trend in the arsenotherapy of syphilis is to concentrate the curative dose in the shortest possible time. The highly publicized five-day treatment stimulated some much needed investigations. The old standard eighteen-month continuous alternating system, although efficient and relatively safe, was unsatisfactory in that throughout the country probably not more than 15 per cent of those with early syphilis received what was considered to be adequate treatment. Shortening the time of treatment may be expected to increase this figure.

Many modifications of the five-day treatment have been advocated; one-day drug and fever, five-day intravenous drip, ten-day multiple injection, and thirty-day, eight-week, ten-week and twelve-week schedules, all designed to give a curative dose of Mapharsen. It is known that a given

amount of Mapharsen has a definite therapeutic index, whether given in five days or several weeks, but that the shorter the time the greater is the risk of toxicity.

All systems of arsenotherapy cause a certain amount of morbidity, most of which is mild but nevertheless undesirable. No cases of morbidity as the result of penicillin therapy have been reported. This fact seems to be of great importance to the armed forces. If it should be established that penicillin is as efficient as the arsenicals, a great advance in medicine will have been made.

* * *

Although gonorrhea and syphilis are still important causes of morbidity in the armed forces, they are relatively less so than in any previous mobilization. This is due first to the fact that the Army and Navy both have capable organizations whose specific job it is to control venereal disease, and second to the immediate utilization by the services of the almost unbelievable advances that are being made in the therapy of these diseases.

Morbidity from venereal disease can be further reduced. This would mean fewer noneffectives in the armed services and on the home front. It is unquestionably our duty to bring this about at this critical time when it is imperative that we do our utmost to eliminate everything that may impede victory.

1101 Beacon Street

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SURGICAL EXPERIENCES WITH THE WOUNDED OF THE BUNA CAMPAIGN*

COLONEL AUGUSTUS THORNDIKE, M.C., A.U.S.

MAJOR General Norman T. Kirk, the Surgeon General of the Army, has stated that out of every 100 wounded in battle in this war 97 may be expected to survive. This is truly a glowing tribute to modern military medicine. All those who have husbands, sons or brothers in combat may take heart and gain great hope that their nearest of kin, if wounded, have a very good chance of returning home. It is my duty to report any thoughts and any facts that we with overseas experience in military service can pass on, even though they concern a minor fraction of the total experience in caring for the sick and wounded of the Army.

The title confines my remarks to an action with the enemy — the first participated in by our Army ground forces that occupied a period of approx-

imately twelve weeks from early November, 1942 — the Buna Campaign in New Guinea. On reaching the continental United States it seemed strange that little general interest had been gained concerning the Southwest Pacific theater. To be sure, the action to be described was not one participated in by large bodies of troops, but it was an important engagement, and particularly so in respect to the soldiers who were taking part in it. Those decorated with the Purple Heart will never forget that experience — they carry scars that have a meaning. The nearest of kin of those killed will remember this engagement. Good surgery near the line of combat saved many lives. Native litter bearers performed heroic service in evacuating the sick and wounded on hand-hewn litters. Up to this date the Fifth Air Force has evacuated more than

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gonococci in women. No woman who admits a sexual contact and who has been identified as a possible source of a known infection should be diagnosed as not infected, no matter how normal she may appear on inspection, without at least one negative culture. The Massachusetts Department of Public Health will shortly announce a new regulation to the effect that whenever a woman is alleged to have been exposed to, or to have been, the source of a gonococcal infection the department shall require that there be one or more negative cultures of material taken from the urethra and cervical canal before it will accept a report that the person is free from infection. As a matter of fact, it would be a wise public-health measure to give a five-day course of sulfathiazole to all women who admit a recent exposure to a known case of gonococcal infection, regardless of negative laboratory findings. If this were done, many infections now overlooked would be cured, and this would probably lower the rate of infection in the services.

There have been no advances in therapy that are more electrifying than the newer methods of treating gonorrhea and syphilis. With the introduction of the sulfonamides from two thirds to three fourths of gonococcal infections were cured within two to five days, whereas previously cure had taken from two to five months. Today more than 95 per cent of all gonococcal infections, sulfonamide-resistant and sulfonamide-susceptible, can be cured with penicillin in eight to ten hours.

Frequently there is a considerable lag between the announcement of a new discovery by laboratory and clinical investigators and its adoption by the medical profession. There has been no hesitancy by the armed forces in adopting newer treatment methods for venereal disease. Existing methods have been altered immediately as soon as clinical trial has demonstrated something more efficient. For this the services are to be commended. Inasmuch as the armed forces are said to have an adequate supply of penicillin, it may be that in the near future all gonococcal infections in the services will be treated with this highly efficient agent.

Until a few months ago servicemen with gonococcal infections were given a course of chemotherapy, and if this did not result in cure they were given a second course after an interval of two or three days. Those who were not cured by the second course were, so far as facilities permitted, sent to a general hospital for fever therapy. Fever therapy has now been discarded in favor of penicillin, and it was recently announced that military personnel with gonococcal infections would be given but one course of sulfathiazole, and that if this failed to cure they would be given penicillin without further delay. It may appear fantastic, but it is nevertheless conceivable that the Army could provide facilities in infirmaries where men with gonococcal infections could report at six o'clock in the afternoon, go to

bed and be given an injection of penicillin every two to three hours during the night, and be discharged to duty at 6 or 7 o'clock the next morning, cured of their infections. This would mean that the loss of man power due to gonorrhea would be almost negligible.

Between March 13 and April 30 of this year, 7 patients with sulfonamide-resistant gonococcal infections—60 men and 17 women—were treated with penicillin in the Out-Patient Department of the Massachusetts Memorial Hospitals. Each received a total dosage of 90,000 Oxford units given in divided doses from 9 a.m. to 5 p.m. on the first day and one injection on the morning of the second day. Positive cultures were obtained from every case just previous to the beginning of treatment. Cultures were done at two-hour intervals during the first day and daily thereafter for three days, and then once a week for three weeks. In only 2 cases were positive cultures obtained after the first injection. In one the culture was positive two hours after beginning treatment but all subsequent cultures were negative. In the second case a positive culture was obtained twenty-four hours after beginning treatment but all cultures on succeeding days were negative. Further experiments are being conducted for the purpose of working out a system of therapy whereby it will not be necessary for patients to give up an entire day to the treatment.

With such an efficient therapeutic agent as penicillin, one is justified in looking forward to the day when gonorrhea will be an extremely rare disease. There is much to be done, however, before that time will arrive. A male patient, who reported to us from another clinic and who had had his infection for thirty days, responded immediately to treatment clinically and bacteriologically. Subsequently, following a sex contact with his wife, he became reinfected. Cultures done on his wife were positive, whereupon she was treated with penicillin and the husband was re-treated, with the result that they are both now negative. It will be necessary to get all women now infected under treatment before the job can be completed, and this is something that will take time and perseverance.

There is a trend in military and civilian hospitals to have gonorrhea treated in medical rather than urologic or gynecologic departments. Turner and Sternberg² report as follows:

It can be said categorically, it is in those Army hospitals in which reliance is placed on internal medication and forced fluids to the exclusion of local treatment that the best results are being obtained. Nothing appears to be gained by urethral instillations, prostatic massage or the passing of sounds in the ordinary case of uncomplicated gonorrhea, and the proportion of complications appears to be significantly higher where these procedures are employed.

The Army's experience is similar to that of many clinicians: therefore, the medical department seems to be the logical place for treating gonorrhea.

wounds were infrequent, generally requiring closure of bowel perforations, rarely resection. There is no better criterion of the quality of the early surgery performed than to observe the later convalescence at the general hospital.

No complication of wound healing was more common than fungus diseases of the skin. Many kinds of pathogenic fungi exist in this humid jungle and constantly attack the combat soldier. Figures for tetanus and gas infection are not available.

Five factors played an important role in the care of the sick and wounded of this campaign. All were co-ordinated well, resulting in the saving of many soldiers. Without good surgery at a forward area, without plasma, without chemotherapy, without native carriers and without air evacuation, this could not have been accomplished.

Possibly I should have described the surgical care of the wounded in this campaign. The care of

the wounded soldier, however, involves more than the actual surgical care. The soldier, sailor or marine deserves the best. Perhaps it seems wise to illustrate the philosophy of the soldier by quoting excerpts from a letter written by a marine about to embark for overseas and found on his bed at the staging area after his departure: "Nurture strength of spirit to shield you in sudden misfortune . . . Try not to distress yourself with dark imaginings; many fears are born of fatigue and loneliness . . . And whether or not it is clear to you, no doubt the universe is unfolding as it should." That represents a creed, a faith, a trust and a purpose worth noting. Our soldiers are the best, and they look to the medical department of the Army or Navy for the best service. It is our obligation to determine that the medical service rendered is worthy of this marine's faith and trust. Speaking as one who has seen, it is a privilege to report that the wounded soldiers are receiving the best possible medical care.

MEDICAL PROGRESS

ANTIBIOTICS AND BACTERIOSTATICS IN BLOOD AND BODY FLUIDS

WILLIAM T. SALTER, M.D.*

NEW HAVEN, CONNECTICUT

IN the use of therapeutic agents of a chemical nature, it has become increasingly important to determine the concentration of the drug that circulates in the blood stream. For generations American chemotherapeutic agents have been thought of in terms of dosage, that is, the amount to be injected or ingested at a single administration. The modern concept more closely approaches the European meaning of the term "*dosage*," that is, the concentration of effective agent produced. It is becoming more and more essential to maintain the concentration of pharmacotherapeutic agents within certain limits.

If this is not done, two difficulties may ensue. If the concentration is too low, the drug will not be effective and fastness to the drug may ultimately develop. If, on the other hand, the concentration is too high, the danger of toxic symptoms and untoward side reactions becomes increasingly great. To steer through this Scylla and Charybdis must be the goal of the best therapy in the next decade.

In order to achieve this end, much more attention must be paid to methods whereby the approximate concentrations of circulating therapeutic agents can be determined easily and reliably. There are two general ways in which this can be done: first, the concentration may be determined directly in the cir-

culating blood, preferably in the serum or plasma; second, in certain cases the urine may be viewed as a blood filtrate, when due regard must be paid to the time interval represented by a given sample. Usually the latter procedure is feasible only if the agent is stable and no considerable storage depots exist in the organism.

Although the present article is concerned primarily with antibiotics and bacteriostatics, it should be pointed out that this principle of dosage — in the Continental sense — probably applies to a considerable number of chemotherapeutic agents. It is known, for example, that in the relief of hypothyroidism the ultimate aim is to raise the concentration of circulating "hormonal" iodine to a level approximating 5 microgm. per 100 cc.¹ Similarly, there is evidence that in the use of digitalis glucosides it is not highly satisfactory to know only the amount administered daily.² The desired therapeutic effect will be approached much more closely if one considers the concentration of glucosides circulating in the blood stream.³ Such facts raise the question whether dosage will ultimately be expressed in terms of milligrams or micrograms per 100 cc. of plasma rather than in amounts to be administered at a single moment.

This principle has become so evident in the case of the bacteriostatics and antibiotics, and the antibiotics are of such prime importance in the total war

*Professor of pharmacology, Yale University School of Medicine.

85,000 patients — a larger number than in any other theater.

Perhaps the most valuable development in military medicine in this theater concerning the care of the sick and wounded was the organization, development and operation of the portable surgical hospital. It is appropriate that credit be given to those particular units that pioneered in this early action. The general hospital, with which it was my privilege to serve, provided two such units, each commanded by a member of this society — Major Neil W. Swinton and Major George A. Marks. The portable hospital is a new development of this war, advisedly designated portable since the entire tentage, mess and surgical equipment and medical supply are carried on the backs of the personnel. Jungle warfare in a wet tropical atmosphere handicaps land transport to such an extent that the human pack is the only method of movement in the most advanced forward areas. Wards and operating rooms were tents, and beds were cots or litters elevated above the ground to avoid flooding. The personnel slept in "jungle beds." In the Buna Campaign selection of the site of the hospital was the really important requirement for reasonably comfortable operation of the hospital. Blackout requirements were enforced, and night operating was done with little or no ventilation. Because of the heat, the personnel were stripped to the waist.

Surgical care of the wounded was first carried out on the field of battle, where necessary dressings were applied; litters then bore the patient to the rear. Emergency care and necessary splinting were provided at the battalion aid station. From there, by litters or walking, depending on the location and type of the wound, the wounded were carried or directed to the portable surgical hospital, where major surgery or fracture reduction and splinting, where indicated, was accomplished. The patient was anesthetized, preferably with Sodium Pentothal but sometimes by spinal or local anesthesia. Blood plasma was used entirely as a substitute for whole blood, and saline and dextrose solutions for infusions. Fluid loss in perspiration was a constant factor in the tropics. The drugs used chiefly were the sulfonamides, quinine, tetanus toxoid and morphine. Nursing care was difficult in particular at night, when the only light was that from a hooded flashlight. Feeding patients hot food and caring for the usual sanitary requirements entailed by a bedpan were tedious and most trying tasks. The patients, however, received the best housing and the best medical and nursing care available within hundreds of miles, and remained in the hospital several days or until they could withstand the next stage of evacuation.

In reviewing the surgery later seen at the general hospital, one can but marvel at the results. One wonders why elaborate surroundings are required when such results can be obtained in the most prim-

itive environs. It was proved, however, that good and better surroundings were necessary for wound healing and more efficient bed care for eventual recovery. In other words, for only a few days did the patient gain in his primitive jungle surroundings.

The surgical procedures carried out have been described by Major Marks in a graphic account of his portable surgical hospital, published in the December, 1943, issue of the *Bulletin of the United States Army Medical Department*. At present he is acting as assistant to the surgical consultant in that theater, and doubtless will have more to describe when he returns. In his present assignment, he is putting to practical use his invaluable experience of this early campaign. Major Swinton, now commanding a field hospital at the advance base, will likewise have much to tell.

In considering the types of wounds and the surgery carried on, one should be cognizant of the weapons used by the enemy. Machine guns, small arms, grenades and mortars were the principal weapons employed by the Japanese. What artillery there was, was put out of action early in the engagement. Sniping was the favorite mode of fighting. Therefore, one would expect penetrating bullet wounds to be the most frequently encountered. Wounds of the soft parts were most frequent, many involving the peripheral nerves, bones and joints and about 70 per cent involving the extremities. Less frequently the head, chest and abdomen were hit. The booby trap, if it existed, was not mentioned by those evacuated to our general hospital. Any record of surgery under the circumstances described above should be judged in two phases — the immediate result and the condition of the wounds and fractures when the patient arrived at the general hospital. In both categories it is a pleasure to report a mortality of 3.6 per cent, including all wounded cases at the portable surgical hospital. This proved that excellent surgery had been done. The general hospital patient arrived in excellent surgical condition after over 1000 miles of travel.

Every surgical procedure carried out with the most modern concept of conservative débridement and fracture reduction and with sound judgment, proved to have been correct. The usual procedure for the surgical treatment of wounds consisted in dusting sulfonamide powder into the débrided wound and providing a gauze drain, and encasing the extremity in plaster of Paris slabs. Alignment of fractures at the time of débridement and application of plaster were essential, and only a few of these patients lost position in transit, this being corrected at the next hospital stay. Head wounds did not do so well if above the level of the mandible. Chest wounds were usually penetrating and through-and-through, accompanied by rib fracture and hemothorax and occasionally by infection. Abdominal

ount of the aliquot contained in the sample is 0.5 microgm. Apparently, other methods are used when the concentrations in blood or body fluids are lower than that just described.

Atabrine in blood and body fluids. One of the most useful of the methods suggested is that of Brodie and Udenfriend.⁹ In this procedure, atabrine is isolated from the biologic material being investigated by reaction of the free base at a pH of about 8.0 with ethylene dichloride. The solution is washed free of degradation products of atabrine with 2.5 N sodium hydroxide. The atabrine is then extracted with aqueous concentrated lactic acid. The final determination of the atabrine is performed in the lactic acid by means of its fluorescence.

A simpler method involves estimation of the atabrine through its fluorescence in the original ethylene dichloride solution. Incidentally, it should be remembered that this solvent may prove toxic. This last procedure is recommended for routine clinical use, and is extremely simple and rapid. In this way, even under field conditions, it is possible to know the concentrations of the drug circulating in the blood of each patient.

A similar method suggested by Masen¹⁰ is as follows:

Five cubic centimeters of oxalated blood is mixed with 5 cc. of 4 N sodium hydroxide and 8 cc. of an alcoholic mixture consisting of equal parts of isobutyl and isopropyl alcohol. One cubic centimeter of water and 7 cc. of petroleum ether (B.P. 30-60°C.) are added. Next, 1 cc. of the atabrine standard, containing 63.6 mg. per liter, is added to another 5-cc. sample of the same blood. It is treated similarly and is shaken for five minutes.

The upper alcoholic layer containing the atabrine is removed. Preliminary centrifugation may be needed to break emulsions at this stage. To the upper layer is added 10 cc. of a solution containing 30 per cent isopropyl alcohol in 10 N hydrochloric acid. The lower layer from this combination is saved, and an 8-cc. sample is taken. This is stabilized with 1 cc. of a buffer consisting of 4 gm. of sodium borate in 100 cc. of 1.35 N sodium hydroxide. The final comparison between standard and unknown is made in a fluorometer, according to the following equation:

$$\text{Conc. of unknown (mg. per liter)} = \frac{U}{S} \times \text{standard conc.} \times 200.$$

U being the reading of the unknown and *S*, that of the standard

The fluorometric method for estimating atabrine has been extended by Auerbach and Eckert¹¹ by the use of caffeine sodium benzoate. In the presence of this reagent the fluorescence of atabrine is intensified some fifteen times. With this procedure a 5-cc. sample of blood containing 0.1 microgm. of atabrine yields a significant result. Furthermore, the sensitivity is adequate for the analysis of blood concentrations such as are found under actual therapeutic conditions. A preliminary extraction with ether is required. For best results the temperature must be controlled.

This procedure has been applied to human blood and bloods from the following animals: rabbit, rat, pig and duck. At a concentration of about 4.0 microgm. per 100 cc. of whole blood, the recovery is 96 per cent or better, and the manipulation involved is simple.

Atabrine in urine. It is well recognized that after the administration of atabrine, the urine contains material that emits an intense yellow color and fluorescence. It has been assumed by some workers that this appearance of the urine is entirely due to unchanged atabrine, and this material *in toto* has been determined as a means of measuring the saturation of atabrine in the blood and body tissues. The work of Scudi and Jelinek,¹² however, has shown that a number of acridine derivatives appear in the urine following administration of the drug to experimental animals. The partition of these various acridines varies from species to species, and is different in laboratory animals from what it is in man. Consequently, any method that is to be applied clinically must take cognizance of the fact that the urinary excretion of atabrine is quite complex.¹³ If the excretion products found in the urine were active against malaria, there might not be any objection to treating them as atabrine. Experiments by Seeler,¹⁴ however, have shown that at least one of these fractions is not active against the schizonts of avian malaria at dosages of 20 to 100 mg. per kilogram. Moreover, these concentrates were more toxic than is atabrine.

The method of Brodie and Udenfriend⁹ has the advantage that any decomposition products of atabrine that may also be present are not recorded. In this respect the method is preferable to somewhat simpler methods, such as that of Craig,¹⁵ which also depends on fluorescent material. The use of fluorescence to detect the atabrine endows the procedure with a high degree of specificity. A Coleman glass filter No. B₂, combining both Corning No. 5113 (2 mm.) and No. 3389 (2 mm.), is used to limit the transmission of fluorescent light, and is more specific than Corning No. 5113 alone, which permits greater sensitivity but transmits a considerable amount of fluorescence derived from normal components of biologic materials.

QUININE IN BLOOD, BODY FLUIDS AND URINE

Now that many observers have decided that quinine is not the drug of choice in many cases of malaria, information regarding its pharmacologic fate is being released for general perusal. Intensive work on its behavior in animals and man has been accumulating behind closed doors during the last three years, and some of it — especially work on the related isomer quinidine — will be of permanent and practical interest. Of this large and rapidly appearing literature, only a few significant instances can be cited.

Quinine in blood and body fluids. In 1931, Vedder and Masen¹⁶ demonstrated that the effectiveness of antimalarial therapy depends on the maintenance of certain concentrations of the drug in the circulation. Because the drug disappears rapidly from the blood after intravenous injection,^{17, 18} it is desirable to follow the blood level to ascertain the need for

effort, that it seems desirable to summarize a few of the methods now available for clinical use. At present most of these are limited to large clinics, but there are indications that further simplifications will make them available even to the busy practicing physician so that he may carry on intelligent therapy. Indeed, it seems likely that many of the untoward effects that are reported through widespread use of the sulfonamides could be avoided if the amount of circulating drug were better known in the given case. To many local practitioners this may seem too much to expect, but probably the procedures involved will eventually be no more complicated than are many methods ordinarily used in clinical pathology.

SULFONAMIDE COMPOUNDS IN THE BLOOD, BODY FLUIDS AND URINE

The distribution of sulfonamide drugs in body fluids has been discussed recently in this journal by Davis,⁴ who has discussed the possible mechanisms of their action.

The original method of Marshall⁵ has proved to be so useful in the control of sulfonamide therapy that various modifications and improvements are important. One such advance has been suggested by Scudi and Jelinek.⁶ This latest modification allows the color to be concentrated so that it is possible to measure highly diluted blood filtrates. Because the heterocyclic sulfonamides tend to be adsorbed by protein precipitates, it is especially desirable that protein be precipitated in dilute solution. The device suggested by Scudi and Jelinek consists in extracting the final color produced by the azo-dye reagent with small volumes of butyl alcohol. The method is easily applicable to routine blood analyses.

These authors worked with solutions of sulfanilamide, sulfathiazole and sulfapyridine at concentrations ranging from 0.1 to 0.5 mg. per 100 cc. After the production of the color in the usual manner, they extracted this dye with *n*-butanol. In this way they were able to concentrate the dye and so to increase the intensity of the color produced for a given amount of the bacteriostatic concerned. In the case of sulfanilamide itself, only 90 per cent of the dye was extracted, but in the case of the heterocyclic sulfonamides, production of the color was complete.

This refinement will be useful in studying bacteriostatics that are effective at low concentrations and in studying the distribution of bacteriostatics throughout various body fluids. The principle may also be used in preparing standards for direct visual comparison, as in clinical tests.

In applying this method to various primary aryl amines, it is necessary in each case to use the pure compound in question in the standard. The use of a green filter (Corning, Sextant 63, No. 401, 2 mm. thick) is desirable, especially with weak colors. The routine procedure for oxalated blood as extensively practiced in clinical laboratories calls for 2 cc. of blood. The classic procedure, in brief, is as follows:

Exactly 2 cc. of oxalated blood is delivered into a flask and laked with 30 cc. of saponin solution. After standing for two minutes the blood proteins are precipitated with 8 cc. of 15 per cent trichloroacetic acid in aqueous solution, and the precipitate is filtered off. Ten cubic centimeters of the filtrate is taken for determination of the free drug. To this sample 1 cc. of 0.1 per cent sodium nitrite is added, and the combined solution is allowed to stand for three minutes at 0° C. or at some known temperature. Next, 1 cc. of a 0.5 per cent ammonium sulfamate solution is added to exhaust the excess of nitrite. After two minutes, 1 cc. of the solution of *N*-(1-naphthyl) ethylenediamine dihydrochloride is added. The color develops rapidly.

The newer method of Bratton and Marshall,^{7,8} which employs *N*-(1-naphthyl) ethylenediamine dihydrochloride, has now been adapted to the following sulfonamide derivatives: sulfanilamide, sulfapyridine, sulfathiazole, sulfaguanidine and sulfadiazine. For use with sulfamerazine and other compounds, certain modifications are necessary, but these are not yet standardized. The unknown is compared with an appropriate standard that has been treated as described above. It is convenient to set the 1-mg. (per 100 cc.) standard at 10 mm., the 0.5-mg. standard at 15 mm., and the 0.2-mg. standard at 20 mm. depth in the Duboscq colorimeter. This comparison can be made immediately, and if solutions are kept in the dark, no change in color is observed for an hour or more. To determine the total drug, 10 cc. of the filtrate is treated with 0.5 cc. of 4 N hydrochloric acid, heated in a boiling water bath for one hour and cooled, and the volume is adjusted to 10 cc. The subsequent procedure is as stated above for determining the free drug.

If the urine is used as a rough indication of blood concentration, it should be acidified and diluted so that the final concentration is 1 or 2 mg. per 100 cc. The diluted urine can then be compared with the usual standard solutions for blood, as described by Bratton and Marshall.

ATABRINE* IN BLOOD, BODY FLUIDS AND URINE

The present restrictions on methodology in the use of antimalarials — restrictions that apply even to the simplest of almost self-evident facts — prevent any detailed discussion of the aims that are to be desired in the use of atabrine, either in the suppression or the treatment of malaria. One can only quote material published in the general literature, such as the following:

Information on the plasma concentrations of atabrine in either of the latter conditions should prove as helpful in the quantitative control of such therapy as is information on the plasma concentration of the sulfonamides in the control of sulfonamide therapy.⁹

One is not allowed to divulge the concentrations required to produce effective therapy or suppression, but one does note from the published literature that the available methods are applicable when the concentration is at least 50 microgm. per liter and the

*Although the term "atabrine" has been superseded in the *United States Pharmacopoeia XII* by the term "quinacrine hydrochloride," the older term has been retained in this article because of its general contemporary use.

One of the most convenient of these newer procedures is that of Sherwood, Falco and de Beer.²⁷ The authors have informed me that it should prove satisfactory for blood provided the standard dilutions of penicillin (used for comparison) also contain an equivalent amount of blood. In this method, 5 cc. of nutrient agar (pH 7.0) containing 200,000 *Bacillus subtilis* spores per cubic centimeter is poured into a Petri dish, and after the agar has solidified, four sterile filter-paper disks (15.3 millimeters in diameter) are spaced evenly upon its surface. These disks are used to absorb and retain the samples under test. Four plates are employed, each testing simultaneously two dilutions of the standard (S) and two of the unknown (U). The weaker of both dilutions should be one fourth, as concentrated as the stronger. Each of these four samples is placed on one of the paper disks and allowed to soak into it. In taking small samples of the four liquids, it was found that a bacteriologic drop was nearly as accurate as a micropipette. The drop had the advantage that it was more readily cleaned and prepared for use. After some five hours of incubation at 37°C., the colonies of *B. subtilis* should have grown sufficiently to delineate clear zones of inhibition. The diameter of this zone should be measured to the nearest millimeter, and the sums of the four zones of inhibition produced by the standard (S₁) and weak standard (S₂) and by the unknown (U₁) and weak unknown (U₂) should be ascertained by addition.

The potency of the unknown (U) with reference to the standard (S) can be calculated from the following equation,

$$\text{Potency} = \text{antilog} \left\{ 2 + d \frac{(U_2 + U_1) - (S_2 + S_1)}{(U_2 - U_1) + (S_2 - S_1)} \right\}.$$

In this equation, *d* signifies the log of the ratio of the greater dose to the smaller dose. This type of assay is statistically sound and convenient. It deserves a careful trial with blood and other body fluids.

In applying this method, it is necessary to control a number of variables that affect the answer. Among these are the temperature and duration of incubation, the size of the disk, the depth of the agar, the volume of the dose and the number of *B. subtilis* spores per plate. If these factors are maintained constant, however, the results are satisfactory for most biologic problems.

Recently Goth and Bush²⁸ have suggested a rapid method for the estimation of penicillin. This is based on the finding that the antibiotic inhibits the production of nitrite from nitrate by cultures of *Staphylococcus aureus*. This test can be carried out in less than ninety minutes. Furthermore, its accuracy is greater than that of the serial dilution method commonly used.

The test strain of *Staphylococcus aureus* is grown for twenty-four hours in a special peptone medium and then diluted with a medium containing peptone,

sodium nitrate and *p*-aminobenzoic acid. A standard preparation of penicillin is used as a control tube and treated in the same fashion as the unknown. After sixty to ninety minutes' incubation the concentration of nitrite is determined.

The determination of the nitrite formed is based on the method of Shinn.²⁹ A trichloroacetic acid filtrate is treated with *N*-(1-naphthyl)ethylenediamine dihydrochloride. The resulting color is determined after three minutes in a photoelectric colorimeter with a green filter (Cenco No. 525P). Because an excess of *p*-aminobenzoic acid is present, the intensity of the color developed in this diazotization process is determined by the concentration of the nitrite present. Appropriate standard solutions containing known concentrations of nitrate are used as the basis for comparing the control tube with the unknown. Obviously, it is essential that all cultures be incubated for the same time at the same temperature.

Rammelkamp³⁰ has also described a simple method for determining the concentration of penicillin in body fluids and exudates. Because hemolytic streptococci are four to sixteen times as sensitive as staphylococci, an especially sensitive Group A strain of hemolytic streptococcus isolated from a case of erysipelas was chosen. Broth cultures at twelve hours (in veal infusion with 1 per cent erythrocytes) were diluted so that the number of organisms per cubic centimeter ranged from one thousand to ten thousand. Half a cubic centimeter of this dilution was added to each unknown sample, comprising 0.7 cc. total volume. The test tubes were then incubated for eighteen hours and finally examined for hemolysis. By comparing such a series with a series containing known amounts of penicillin, one can estimate amounts as low as 0.0039 Florey unit per 0.2 cc. of solution.

This method is applicable to urine, whole blood, erythrocytes, joint fluid, spinal fluid and exudates from empyema cavities. Unknown samples may be stored at 5°C. for two weeks before testing without serious loss, unless contaminated. In such a case it is wise to sterilize the sample by passage through a Berkefeld or Seitz filter.

Effective concentration. Rammelkamp and Keefer³⁶ studied the concentrations of penicillin in the blood stream required to produce optimal effects. For *Streptococcus haemolyticus* the value was between 0.019 and 0.156 unit per cubic centimeter of serum, whereas for maximum bacteriostatic effect with *Staph. aureus*, at least 0.156 unit was required. Furthermore, whole blood containing 5.1 mg. of sulfadiazine per 100 cc. was less active against streptococci than was whole blood containing 0.7 unit of penicillin per 100 cc. After intravenous (or intramuscular) injection of penicillin large amounts of the drug appear in the urine, even as much as half the injected material. Unfortunately, intravenous injection is not followed by elimination of penicillin

further dosage or to regulate the program of medication. Until recently highly specific methods were available, but these generally involved a time-consuming extraction process. Brodie and Udenfriend,¹⁹ however, have described a simple but precise method probably applicable to human plasma.

The test is based on the strong fluorescence of acid solutions of the alkaloid in ultraviolet light. When the quinine concentration is low, the intensity of emitted light is proportional to the alkaloidal concentration. The absolute concentration is, in fact, too low because of so-called "quenching," but this fault is automatically corrected by using appropriate control standard solutions. In order to avoid serious loss of the drug by adsorption on the protein precipitate, the plasma filtrates are prepared at high dilution by the use of metaphosphoric acid. The final concentration is read in a photofluorometer over the range of 1 to 30 microgm. per 100 cc. Above plasma concentrations of 100 microgm., the method gives very satisfactory results. Moreover, because the filtrates are stable, they can be stored for several days and analyzed in groups. The method is also adaptable to quinidine.

In connection with experimental work on avian malaria, Kelsey, Oldham and Geiling²⁰ have studied the distribution of quinine in the tissues as well as in the blood of fowls after oral administration. These results were compared with the effect of intravenous injection. An interesting finding was a temporary accumulation of quinine in the red cells at a concentration higher than that in plasma. The leukocytes show an even more striking preferential accumulation. The blood rapidly yields up its initial load of drug, so that ten minutes after intravenous injection high concentrations are found in the liver, kidneys, spleen, adrenal glands, lungs and liver. The data serve to emphasize the important fact that quinine is not accumulated in the tissues even after long-continued administration. Quantitatively, the results confirm those in the dog and cat reported by Hatcher and Weiss.²¹

Quinine in urine. The medical services of the armed forces have been obliged to develop simple tests for the detection and rough estimation of quinine in the urine. Such tests are needed to detect those who have failed to take prophylactic medication. They may also be used in a semiquantitative fashion to control suppressive dosage. Independent studies by Cornell and Kaye²² and by Glazko²³ have shown that the double iodide of mercury (HgI_2K_2) can be used directly in urine without preliminary extraction. The precipitate of iodo-mercurate dissolves on boiling, whereas albuminous precipitates do not. If precise results are needed, the turbidity produced can be measured with a photonephelometer. In this case the acidity and the range of concentration of the quinine must be adjusted for best results to pH 2.0 and 1 to 5 mg. per 100 cc., respectively. When 0.6 gm. of quinine sulfate was ingested, it was

found by this method that the urinary quinine excretion rose at four hours to a peak of nearly 25 mg. an hour, and gradually declined to less than 5 mg. after fourteen hours.

Although urinary quinine excretion is variable, approximately 40 per cent of the usual therapeutic dosage is excreted by this route. The excretion is rapid, and after twenty-four hours only a trace appears in the urine.

The excretion of quinine is influenced by several variables, among which the urinary acidity is important. Haag, Larson and Schwartz,²⁴ for example, gave 0.5 gm. of quinine orally to human subjects and found that when the urine was maintained alkaline, half as much quinine was excreted as with an acid urine. At best, however, the resulting conservation of the drug seemed to be less than 10 per cent.

PENICILLIN IN BLOOD AND BODY FLUIDS

In the use of penicillin it is especially advantageous to determine the concentration of circulating antibiotic, particularly in cases being used for statistical studies of the therapeutic results. Penicillin is so rapidly removed from the blood stream and so largely excreted in the urine that an interval of two hours reduces the effective concentration to very low limits.

Some 58 per cent of penicillin is excreted by the kidneys after intravenous injection.²⁵ Rammelkamp and Keefer²⁶ found that this loss occurs largely in the first hour after injection. The effect of Diodrast in preventing the excretion was striking. Whereas about 57 per cent of intravenous penicillin was lost in the course of a few hours, with Diodrast only 32 per cent was recovered in the urine. Despite this conservation of penicillin, however, the blood level became negligible in less than two hours. Without Diodrast, it reached zero in approximately forty-five minutes.

The hemolytic streptococcus is extremely sensitive to penicillin, but even in this instance a concentration of at least 0.15 units per cc. is desirable. Various procedures and various derivatives are being tested in the hope of maintaining a high concentration over a longer period. At present the drug must be administered every two hours in order to hold the blood concentration up to effective levels.

The methods now available for the estimation of penicillin activity are essentially bioassay procedures. Accordingly they involve the usual *bête noire* of biologic variation. This fact implies that for greatest accuracy the answer, in graphic terms, should be read as a *line* rather than as a single point or single value. The new methods for the assay of penicillin take cognizance of this statistical situation, and provide for a matching of the unknown with known standards. Unfortunately no extensive published experience is yet available with this type of procedure as applied to blood.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30451

PRESENTATION OF CASE

First admission. A seven-year-old Negro school-child entered the hospital because of exophthalmos. The child had been in apparent good health until fifteen months before entry, when she seemed to become restless, nervous, irritable and emotional. A month or two later exophthalmos was noted. During the next few months the symptoms progressed, becoming more marked after an attack of measles. She failed to gain weight, although there was an increase in height of 2 inches in six months. About one month before entry, during an examination in a community hospital, a lump was found in her neck and the basal metabolic rate was noted to be +65 per cent.

The patient had had whooping cough at four years of age and chicken pox shortly afterward. There was a question of head injury at fifteen months of age but x-ray films of the skull taken at a community hospital at that time were negative.

Physical examination showed a well-developed and well-nourished girl. There was slight tremor of the tongue. The thyroid gland was symmetrically and uniformly enlarged. No thrills were palpable over the gland, but a bruit could be heard. Exophthalmos was present, and the hands showed a moderately coarse tremor. There was a loud systolic murmur, best heard at the apex but audible over the entire precordium.

The blood pressure was 120 systolic, 60 diastolic. The temperature was 99°F., the pulse 120, and the respirations 25.

Examination of the blood showed a red-cell count of 5,100,000, with 85 per cent hemoglobin. The white-cell count was 7500, with 74 per cent neutrophils. The urine was normal, with a specific gravity of 1.026. The basal metabolic rate was +63 per cent. The serum cholesterol was 127 mg. per 100 cc. A blood Hinton test was negative.

The patient was given 1 drop of a saturated solution of potassium iodide three times a day, and on the twentieth hospital day a right hemithyroidectomy was performed. The weight of the specimen was 8.2 gm., and on microscopic examination it showed hyperplasia. The patient withstood the

operation well, but on the first and third post-operative days there was considerable oozing of blood from the incision and she was given several transfusions. On the fourteenth hospital day the basal metabolic rate was +15 per cent for height and +32 per cent for weight, with a pulse of 96. The patient was discharged on 5 drops of potassium iodide twice a day and was told to return in six weeks for the removal of the remaining lobe of the thyroid gland.

Second admission (six weeks later). Following discharge the patient remained well, gained 10 pounds and was less nervous.

Physical examination was the same as before.

The temperature and respirations were normal, and the pulse was 96. The basal metabolic rate was +43 per cent for height and +54 per cent for weight.

On the second hospital day a left hemithyroidectomy was performed with the removal of 15 gm. of histologically hyperplastic thyroid tissue. Again there was considerable postoperative bleeding. The basal metabolic rate fell to +5 per cent, and the pulse to 78, and she was discharged on the tenth hospital day.

Final admission (eight years later). Following discharge the patient did well for about two years, at the end of which time definite thyroid tissue was again palpable in the neck and seemed to be increasing in size. The basal metabolic rate was +16 per cent for height and +30 per cent for weight, and the pulse was 120. She was placed on 5 drops of a saturated solution of potassium iodide three times a day. During the next two years, tremor and nervousness reappeared, the mass in the region of the thyroid gland definitely enlarged and the basal metabolic rate rose to +23 per cent for height and +34 per cent for weight. At that time she was given 150 r of x-ray therapy for two doses, followed by two doses of 200 r each. During the month after x-ray therapy the basal metabolic rate gradually fell to -17 per cent for height and -13 per cent for weight; the pulse was 66. She then developed a rash and the potassium iodide therapy was discontinued. The thyroid nodule decreased in size and her condition seemed much improved. The patient apparently remained well until three weeks before the final entry, at which time her appetite became poor and she developed polyuria and polydipsia, and began to lose weight. Ten days before entry she appeared tired, "peppless" and sleepy and complained of pain and tenderness in the costovertebral angles. One week prior to admission there was itching of the genitalia and anus, followed by the draining of a perianal "abscess" three days later. Two short episodes of epistaxis occurred spontaneously. The night before entry the patient became drowsy, with frequent attacks of vomiting, and the next morning was difficult to rouse.

*On leave of absence.

into the spinal fluid. It has been assumed that for this reason penicillin administered intravenously is useless in the treatment of meningitis.

Recent work by Rosenberg and Sylvester,³¹ however, has indicated that the blood-brain barrier is altered in cases of meningitis. These investigators injected 8 patients with meningitis intravenously or intramuscularly, in doses ranging from 20,000 to 40,000 Oxford units. One or two hours later penicillin appeared in the spinal fluid in concentrations of 0.03 to 0.35 unit per cubic centimeter. Because the magnitude of this concentration is adequate for blood, the possibility exists that such cases can be treated without intrathecal injection. Further data are needed. Such observations should, of course, be made only under carefully controlled circumstances, but they appear to show that observations in normal subjects do not reflect the situation when inflammation is present.

Various devices are now under test in an effort to maintain effective concentrations of penicillin for longer periods. Some of these involve a modification of the preparation of penicillin, but these experiments are still in the initial stages so far as information is available at present. Another interesting approach, however, has been the depression of renal excretion by agents that are relatively innocuous to the kidney. For example, Rammelkamp and Bradley²⁵ found that the excretion of penicillin by the kidney was inhibited after the injection of Diodrast.

Recently Beyer and his associates³² have investigated a similar use of *p*-aminohippuric acid, which is secreted by the tubular epithelium, as shown by Smith and his associates³³ and by Bing.³⁴ Experiments in dogs conducted by Beyer and his associates showed that when the plasma level of the hippuric acid derivative is maintained at between 20 and 30 mg. per 100 cc., penicillin is retained in the blood at effective concentrations for appreciably longer periods. Thus, in the control experiments after a single injection of 10,000 Oxford units, the antibiotic was no longer detectable in the plasma after two and a half hours. In animals treated with the hippuric acid derivative, however, detectable concentrations of penicillin persisted in the plasma for three and a half hours. Simultaneously the renal clearance of penicillin from the blood and its recovery in the urine were decreased. Toxicologic studies have shown in mice, rabbits and dogs that *p*-aminohippuric acid is remarkably nontoxic, so that a cautious trial of its use with penicillin is desirable in view of the higher concentrations possible and the increased economy of therapy.

The methodologic aspect of controlled chemotherapy has been stressed in this survey because it is too often neglected. Any clinical report is of little scientific value if it claims that penicillin is ineffective without giving evidence that the concentration in the circulating blood has been maintained adequately high and for an adequately long period. At this stage of knowledge regarding penicillin and other antibiotics, the necessity for constant control

of concentration in the blood cannot be emphasized too strongly.

SUMMARY

If the antibiotics and bacteriostatic agents now available are to be used effectively, their circulating concentration must be known and controlled. Simple methods are now available that can be applied to blood, urine and body fluids. Unless such a check is used in critical cases, it is unwarranted to conclude that the therapeutic agent under test is ineffective. This precautionary procedure is also necessary in most cases to guard against toxicity due to overdosage.

333 Cedar Street

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BUTLER: One can have local irritation from glycosuria. I have never seen perianal in children with diabetes. I do not know or not they occur in adults.

Epistaxis makes one wonder whether there is generalized infection, hypertension or rheumatism. I do not recall epistaxis in diabetes, in diabetes mellitus or in Addison's disease. Tenderness in the costovertebral angle was again elicited on physical examination. I should know how well or poorly this patient was doing.

COTZIAS: She was well nourished.

BUTLER: The draining perianal abscesses on the apparently were not superficial, since pus was obtained on incision. One wonders whether a skin test was done.

COTZIAS: Not during the time that we were here.

BUTLER: There was no evidence of infection. Are there any abscesses in the perianal region. Are there any other records of blood pressure? Is there any evidence that she had a hypertension during the dehydration.

COTZIAS: I do not recall.

BUTLER: If a person with diabetes mellitus ingests food, the resulting starvation leads to overproduction of ketone bodies and acidosis develops rapidly. If such a person then begins to drink the combination of glycosuria, ketosis and dehydration fluid by vomiting quickly produces dehydration. In the presence of such dehydration the hands and feet are usually cold, the circulation is poor and the temperature not elevated, but the temperature subsequently becomes elevated as the patient is rehydrated. Hence, the temperature of 102°F. on admission suggests infection. The pulse was 140. One wonders whether the pulse was poor and rapid.

COTZIAS: The pulse was poor.

BUTLER: That probably reflected the dehydration, possibly an overwhelming infection. The leukocytes were 45 and Kussmaul in character. Examination of the blood showed a red-cell count of 5,140,000, with 15 gm. of hemoglobin. "Dehydration may produce a normal red-cell count when actually there is anemia. The white-cell count was 35,000. That is high but not impossibly high for just dehydration. It does, however, make me think of infection.

Examine the urine examination was done on a random specimen. We have to assume that there is no albuminuria and that it was not just from contamination of a voided specimen. The leukocytes may reflect a cystitis. The blood sugar was 500 mg. per 100 cc., which is average for diabetic coma. I take it that no casts were seen, and that is against nephritis.

Positive story, positive physical findings, and positive blood sugar and positive tests for urine

sugar, diacetic acid and acetone in a dehydrated patient indicate diabetic acidosis. Kussmaul breathing confirms the suggested metabolic acidosis.¹ It tells one that the blood carbon dioxide content is low. I suggest that a whole blood or serum carbon dioxide determination in such a patient is relatively uninformative.¹

Suppose this child had salicylate poisoning instead of diabetes mellitus and diabetic coma. Then the hyperventilation would have been due to the toxic action of the salicylates on the respiratory center; the carbon dioxide content would still have been low, — perhaps not this low, — but the patient would have had an alkalosis, not an acidosis.¹ So the carbon dioxide determination does not even tell whether the patient had acidosis or alkalosis, unless one has used one's common sense as regards the history and physical findings. When one has done so, a carbon dioxide determination contributes practically nothing. Even in a quantitative sense it adds little of clinical importance, since the Kussmaul breathing indicates the extent of the acidosis.

So I should not have asked for a carbon dioxide determination. But I should have asked for a non-protein nitrogen test, since this child possibly had renal disease, and I think that her care in the next twenty-four hours would have been facilitated if it was known whether or not she had renal disease. A high nonprotein nitrogen level on admission might merely have been due to the dehydration. But after the child was hydrated and a good urine volume was obtained, a second test would have shown the part that renal disease played in the picture. I should also rather have had a serum protein than a serum carbon dioxide, because the patient was sure to be given a lot of parenteral fluids. The concentration of the serum protein would have provided information concerning the patient's nutritional state and her ability to handle parenteral fluids. If the serum protein was elevated, fluids could have been given parenterally without danger of edema unless there was a lot of infection. If the serum protein concentration was not elevated in the state of dehydration, one could have been sure that it would be lower after hydration and hence would have been careful about edema as parenteral fluids were given.

I am going to pass over the insulin therapy. I do not believe that the amount of insulin given is really the important factor. One should give enough and not too much. The main thing is the manner in which this patient was supplied with the immediate metabolic needs of fluid and with other substances, including insulin. In the first two hours of therapy the blood sugar fell from 500 to 330 mg., and the acetone was somewhat less, perhaps because all the urine analyses were qualitative — not only in terms of chemistry but in terms of urine volume. I am sure that when the tests for acetone and sugar were done no account

Physical examination showed a semicomatose, dehydrated girl with typical Kussmaul respirations at a rate of 45. Considerable tenderness was present in both costovertebral angles. A draining abscess was present on each side of the anus; both, however, appeared to be quite superficial. Examination was otherwise negative.

The blood pressure was 130 systolic, 70 diastolic. The temperature was 102°F., the pulse 140, and the respirations 45.

Examination of the blood showed a red-cell count of 5,140,000, with 15 gm. of hemoglobin. The white-cell count was 35,500, with 84 per cent neutrophils. Examination of the urine showed a specific gravity of 1.020, a reaction of pH 6, a + test for albumin, a red test for sugar, a +++ test for diacetic acid and a +++ test for acetone; the sediment contained 10 to 15 red cells and 50, to 60 white cells per high-power field. The blood sugar was 500 mg. per 100 cc., and the carbon dioxide combining power 5.7 millimols per liter.

Over the next two hours the patient was given 150 units of insulin subcutaneously and 300 units intravenously in divided doses, with the result that the blood sugar dropped from 500 to 330 mg., the test for sugar in the urine changed from red to brown and the acetone became noticeably less (+++). Over the next four hours the test for sugar in the urine changed to green, with a + test for acetone. Only 80 units of insulin were given subcutaneously over that period of time. During the first six hours she received intravenously 4500 cc. of a solution consisting of two-thirds isotonic saline solution and one third 1/6 molar sodium lactate solution, as well as 250 cc. of plasma. At the end of that period the urine showed only a faint test for acetone and a negative test for sugar. She was more responsive, and the respirations were 35 and approximately normal in depth. The measured urine output during that period was 1560 cc., but it actually was greater since a considerable amount leaked around the catheter.

On admission 1000 cc. of clear fluid had been aspirated from the stomach; the tube was left in place, and the viscus was kept empty by frequent aspirations. At the end of five hours 25 cc. of broth was introduced through the tube into the stomach; this was repeated at half-hour intervals and was well tolerated. The perirectal abscesses were opened, about 20 cc. of pus being obtained. The patient was then given 1000 cc. of 10 per cent dextrose in isotonic saline solution, along with 40 units of insulin, over one and a half hours. The test for urine sugar, however, was brown, and that for acetone +++. At that point the patient became less responsive and the respirations assumed a peculiar gasping quality. Isotonic saline solution containing 2.5 gm. of sodium sulfadiazine was given intravenously because of persistent leukocytosis and a fever of 101°F.; the

volume was 2000 cc. over the next five hours making a total of 6850 cc. of parenteral fluids. The urine output continued to be approximately 200 cc. per hour. The insulin dosage was between 30 and 60 units an hour from the eighth to the twelfth hour of hospital stay, at which time the test for urine sugar became negative. Subsequently only small doses of insulin were introduced, the total dosage of regular insulin being 810 units. The patient became acetone free from the tenth hour on.

Gasping respirations continued, however, and the patient remained semiresponsive. The blood pressure was constant at 130 systolic, 70 diastolic, except for occasional transient rises to 150 systolic, 70 diastolic; one and a half hours before death it rose to 160 systolic, 100 diastolic. The pulse never dropped below 120. At no time was peripheral or pulmonary edema evident. The white-cell count varied from 27,000 to 29,000. Sixteen hours after entry the patient suddenly became unresponsive, and expired fifteen minutes later.

DIFFERENTIAL DIAGNOSIS

DR. ALLAN M. BUTLER: This is an example of hyperthyroidism in childhood, which is frequently extremely serious. Because hyperthyroidism in childhood is so rare, and since most pediatricians know so little about the condition, when they encounter a case of hyperthyroidism they had better send it to a physician for adults who knows hyperthyroidism rather than attempt to treat the case themselves.

I shall start discussing this case at the third admission, eight years after the original admission. The patient was then fifteen years of age. At that time she again had a recurrence of the symptoms of hyperthyroidism in spite of two subtotal thyroidectomies. The decision was made to irradiate the thyroid gland, following which the manifestations of the hyperthyroidism disappeared. Since we are not told much else about the child's thyroid condition, I assume that there were no further symptoms of hypothyroidism.

The development of polydipsia, polyuria, loss of weight and change in appetite usually means one of three things — renal disease, diabetes mellitus or diabetes insipidus, with or without brain tumor. It may possibly mean Addison's disease.

I should like to know whether the child was constipated.

DR. GEORGE C. COTZIAS: She was not constipated.

DR. BUTLER: Usually with dehydration resulting from untreated diabetes, the patient becomes constipated. Abdominal pain, probably due to the dry, impacted feces that result from dehydration and constipation, is not uncommon. But this patient was not constipated, and the pain and tenderness were in the costovertebral angle according to the record — not in the abdomen. Is that correct?

DR. COTZIAS: Yes.

thyroidism, although she may have had a mild . We have seen older people who have a degree of diabetes with hyperthyroidism. As this patient had a fairly severe diabetes, wondering if she did not have persistent thyroidism right through, which accounted for the sudden development of a severe grade of diabetes. Ordinarily, when a person has diabetes mild or severe degree and hyperthyroidism, there is practically no diabetes left after the latter is treated, so that unless diabetes had been present long time or unless the hyperthyroidism had been worse, we have to assume that the diabetes was a new development. On the story, I should think that the patient was cured so far as the hyperthyroidism was concerned and that she developed diabetes de novo. I did not see her during the last episode.

CLINICAL DIAGNOSES

Diabetic coma.
Perirectal abscesses.

DR. BUTLER'S DIAGNOSES

Perianal abscesses.
Diabetes mellitus, with acidosis.
Cellular depletion.
Cardiac failure.
Cystitis?
Glomerulonephritis?
Pyelitis?

ANATOMICAL DIAGNOSES

Diabetes mellitus.)
Diabetic coma.)
Hydropic degeneration of islets of Langerhans of pancreas.
Lymphocytic infiltration of pancreas.
Pneumonia.
Perianal abscesses.
Acute cystitis.
Pulmonary atelectasis.
Thyroiditis.)
Surgical scar: thyroidectomy.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The last basal metabolic rate three years before entry and was normal, $+2$ per cent. Autopsies on patients with diabetes, as Dr. Butler has mentioned, are usually unsatisfactory. We are rarely able to diagnose the exact cause of death. In many cases, infection is the underlying factor that puts the patient into a coma.

In this child I should think the severe perianal infection probably started the ball rolling and ended in coma. There was a lot of perianal infection at the time of autopsy, as well as scattered foci of bronchopneumonia. We were able to get a piece of thyroid tissue, which showed no

evidence of activity; the abnormal histology was perhaps due to irradiation, such as we have seen in other cases. The pancreas was about normal in size and on section showed something that I had never seen before—a fairly diffuse lymphocytic infiltration throughout the parenchyma, which for the most part did not involve the islets. Not having seen many cases of diabetes in children, I talked to Dr. Shield's Warren; he also had never seen this type of lymphocytic involvement. I believe that we have to assume that it was just the result of a mild chronic pancreatitis, because in addition to that there were numerous areas of fibrosis and destruction of the acinar tissue. The islet cells themselves were about normal in size and number, but in many there was definite hydropic degeneration, the type of change that one sees in acute, severe diabetes in children. There was also a mild cystitis and pyelitis, but no evidence of kidney disease. The glycogen stains showed what we expected to find—deposits of glycogen in Henle's tubules in the kidneys and a liver almost completely replaced by glycogen.

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CASE 30452

PRESENTATION OF CASE

A sixty-two-year-old housewife entered the hospital because of severe pain in the back.

So long as she could remember, the patient had experienced low back pain radiating down the posterior aspects of both legs to the heels. The pain was intermittent and lasted for days. Occasionally it occurred after lifting or carrying heavy bundles, but this was not the rule. Six months prior to entry the pain increased in intensity and frequency and was severer in the right leg than in the left. She had frequent muscle cramps in the right leg. According to one statement the pain always started on the right side, and when severe, it was also felt in the left leg. At times the pain was severe enough to require codeine. There was paresthesia of the small toe of the right foot.

Physical examination showed a moderately obese woman who experienced severe distress on motion. The heart, lungs and abdomen were normal. There was slight tenderness in the lower lumbar region. Straight leg-raising on the right was limited to 35° and produced pain down the back of the leg to the heel. On the left it was limited to 60° , with pain down the back of the leg to the knee. Forward bending was limited, and the fingertips could be brought to within only 40 cm. of the floor. The lumbar spine was moderately flattened. Jugular compression did not cause pain. The right

was kept of the relation of the qualitative tests to the quantity of the urine. Hence, all were qualitative.

The acetone determination warrants one comment. A patient in recovery from diabetic coma should not become free of glycosuria before the ketonuria has been cleared up. The persistence of ketosis means the continuation of starvation, which is the cause of the ketosis. The ketosis is a factor in the diabetic acidosis, nausea, dehydration, and so forth. The starvation must be corrected before the ketosis can be stopped, and the only means of stopping starvation early in treatment is the administration of glucose with adequate insulin. Hence, enough glucose should be given so that the urine does not become sugar free until the ketosis has stopped.

"During the first six hours she received intravenously 4500 cc. of a solution consisting of two-thirds isotonic saline solution and one-third 1/6 molar sodium lactate solution, as well as 250 cc. of plasma." That solution, in my estimation, is the correct solution to give in the early stage of repairing the extracellular fluid loss in diabetic coma.¹ The concentration of sodium chloride and lactate (or potential bicarbonate) in such a mixture prevents the continuation of the acidosis while hydrating a patient who is so dehydrated that the kidneys will not function correctly. If one gives physiologic saline solution instead of this combination of two solutions one is administering a solution that, in terms of serum, is hypertonic in chloride by 50 milliequiv. per liter.¹ Physiologic saline solution also has no bicarbonate. The result of giving physiologic saline solution to a patient whose kidneys are handicapped by the poor blood flow incident to dehydration is an elevation of serum chloride and a continuation of the acidosis. To continue for hours the Kussmaul breathing and resultant muscular exertion in a diabetic patient who has suffered severe starvation, severe dehydration and severe cardiac and circulatory embarrassment is not good therapy. The particular combination of sodium lactate and saline solutions is good because it provides an approximately normal plasma chloride concentration — 100 milliequiv. per liter — and a bicarbonate or potential bicarbonate (according to whether one uses sodium bicarbonate or sodium lactate) concentration of approximately 50 milliequiv. per liter, which is double the normal. So immediately there begins a correction of the alkalosis; almost immediately the respirations improve, and in an hour they will be rather markedly improved. Such an infusion cannot do harm. If it puts the patient to rest, it must be good. As soon as the respirations are eased, physiologic saline solution can be used in place of the combined solution.

I am not sure that the disappearance of sugar from the urine meant that the blood sugar had returned to normal, for this patient may have had

renal disease and a hyperglycemia without glycosuria. Whether or not she had renal disease, I should have favored using intravenous glucose after a couple of hours of hydration therapy, since the maintenance of hyperglycemia favors the utilization of glucose and starvation can be stopped only if there is a utilization of glucose. The work of Mirsky² shows that hyperglycemia improves the utilization of glucose. There is no evidence that maintaining the blood sugar above normal does harm provided that something is done about hydrating the patient and that the urine volume is adequate, as it was in this patient. Thus, after two hours of therapy 5 per cent glucose might have been started intravenously, later increasing the glucose to 10 per cent and using insulin in liberal doses while giving the glucose. Glucose administered beyond the rate of immediate oxidative utilization builds up the depleted glycogen stores. Unless this is done, the high blood sugar and the ketosis are difficult to control.

There were no signs or symptoms of pulmonary edema or cardiac failure during the parenteral therapy, since the rate and volume were not excessive.¹ Yet this patient died in the same manner that patients with diabetes sometimes do; that is, after considerable hours of therapy and improvement, they suddenly fail rapidly and die. Analyses show that the serum sodium, chloride and carbon dioxide and the blood sugar were satisfactory. The urine sugar and ketosis had cleared up. Yet she died. I do not know why, but possibly Dr. Castleman can tell us. In this particular case a renal infection or a pre-existing nephritis may have been a factor. Because there is no record of urine cultures and nonprotein nitrogen determinations and because of the presence of perianal infection I do not know whether there was renal infection or nephritis.

In the interest of possibly improving the treatment of such patients, attention should be called to the fact that for sixteen hours this starving patient was given nothing but water, sodium chloride, glucose and insulin, with the exception of a few ounces of meat broth. Extracellular fluid and a total of only 100 gm. of glucose, providing 400 calories, were given this depleted patient. Possibly another 90 gm. of glucose from the body was oxidized to provide an additional 360 calories, but no intracellular constituents were given with these 760 calories to provide for cellular activity or repair. Such is the custom. It ignores the fact that extracellular repair does not restore intracellular depletion, nor does it provide substances essential to the life of cells and patients.

DR. BENJAMIN CASTLEMAN: Dr. Lerman, would you like to say something about the relation of diabetes to exophthalmic goiter.

DR. JACOB LERMAN: Presumably this child did not have diabetes at the time she was treated for

DR. SAMUEL LOWIS: The fact that the patient had pain on lumbar puncture at two different levels favors tumor rather than a ruptured disk. Furthermore, a ruptured disk would not be so large as this lesion.

CLINICAL DIAGNOSIS

Ruptured intervertebral disk?
Tumor of cauda equina?

DR. MICHELSEN'S DIAGNOSIS

Neurofibroma of cauda equina?
Ependymoma of cauda equina?

ANATOMICAL DIAGNOSIS

Neurofibroma of cauda equina.

PATHOLOGICAL DISCUSSION

DR. KUBIK: Dr. W. J. Mixter operated on this patient. He started out by taking off the lamina of the fourth vertebra and came down on a tumor beneath the dura. The tumor, which was found to extend from the lower margin of the lamina of the second lumbar vertebra to the upper margin of the lamina of the fifth lumbar vertebra, was removed except for small bits that were adherent to one or two of the spinal nerves of the cauda equina. Histologically it was a neurofibroma.

The patient made a good recovery, but still has some pain. It is rather interesting, considering the large size of the tumor, that the abnormal neurologic findings were not pronounced, but this is not unusual. We have had cases of both neurofibroma and ependymoma in that locality with no abnormal neurologic findings.

ankle jerk was absent, but the neurologic examination was otherwise negative.

The blood pressure was 150 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a white-cell count of 8500. The urine was normal. A blood Hinton test was negative.

Anteroposterior and lateral films of the lumbar spine showed flattening of the lumbar curve and a list to the left between the fourth and fifth lumbar vertebrae. The interspace between these vertebrae was markedly narrowed, and there were degenerative changes at this level and between the fifth lumbar vertebra and the sacrum, with increased density of the margins of the vertebral bodies.

Lumbar punctures at the third and second interspinous spaces caused unusually severe pain. Only a few drops of spinal fluid were obtained. Because of the pain further attempts at lumbar puncture were not made.

On the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. JOST MICHELSEN: At first glance this seems to be a story of a ruptured intervertebral disk in the lower lumbar region on the right side. For many years the patient had intermittent pain low in the back and in both legs, more so on the right side. The pain was severe and was exaggerated by certain activities. It occurred after lifting or carrying bundles. It was associated with paresthesia of the small toe on the right. There was limitation in forward bending. The lumbar spine was flattened. The right ankle jerk was absent. All these facts are consistent with a ruptured disk in the lower lumbar region.

I shall disregard the x-ray findings of narrowing of the fourth lumbar interspace. It may be found as an incidental observation in patients with no symptoms. The evidence of proliferative changes at the fourth and fifth interspaces is also of little significance for the diagnosis of the level of the lesion.

The paresthesia of the right small toe and the absence of the right ankle jerk indicate that the right first sacral posterior nerve root was involved. Consequently, if the lesion was a ruptured disk it was a protrusion at the lumbosacral interspace on the right side.

The question arises whether this was a ruptured disk. For several reasons I have a notion that it was not. I am inclined to believe that the severe pain that was observed during the lumbar puncture and the fact that only a few drops of cerebrospinal fluid were obtained are significant. I assume, of course, that the lumbar puncture was well executed. The pain, as well as the small amount of

fluid, suggests that there was an intradural mass. On reviewing the history with this possibility in mind one gets the impression that the pain that the patient had had for so many years was not of true mechanical nature. It is said that occasionally it occurred after lifting or carrying heavy bundles, but that this was not the rule. Intermittent spells of pain lasting for only a few days would also be somewhat unusual for a ruptured disk. This is all I have to go on, however, when I suggest the possibility that the lesion was an intraspinal neoplasm.

If there was a tumor, I presume that it had been present for a long time. This is against a malignant lesion. Of other lesions, I should consider neurofibroma, meningioma and ependymoma. Meningiomas in the lumbar area are extremely rare, and I have never heard of one in this area. Ependymomas frequently occur in the cauda equina region. With the long duration of symptoms, however, one would expect widening of the spinal canal, destruction of the pedicles and erosion of the posterior portion of the vertebral bodies at the site of the lesion and probably definite signs of compression of the cauda equina. This leaves us with the third possibility, which is the likeliest. Neurofibromas are the most frequent of the neoplasms of the spinal canal. These nerve-sheath tumors vary in size. It is possible that the tumor originated from the first sacral posterior root on the right and expanded slowly to produce the cerebrospinal-fluid disturbances and displacement of nerve roots, which led to the difficulties that were encountered on lumbar puncture.

I admit that I am unable to make a definite diagnosis of the type of the lesion and only an approximate diagnosis of its true seat. I believe that the patient had an intraspinal lesion in the lumbar area, either a large ruptured disk at the lumbosacral interspace or an intradural neoplasm in the region of the cauda equina. I favor the diagnosis of a neoplasm, either an ependymoma or, likelier, a neurofibroma.

DR. AUGUSTUS S. ROSE: I was wondering if the absence of sphincter difficulty is of any significance.

DR. MICHELSEN: As I tried to point out, it is particularly against an ependymoma. The lesion was probably a neurofibroma.

DR. JAMES B. AYER: Is the absence of sensory findings against neurofibroma?

DR. MICHELSEN: The fact that the only sensory disturbance was a paresthesia of the right little toe is extremely significant.

DR. CHARLES S. KUBIK: Paresthesias are of no assistance in diagnosing the nature of the lesion, but they do help to localize it.

DR. MICHELSEN: That is correct.

DR. AYER: I admit that it is possible for a large ruptured disk lying in the canal to cause paresthesia.

in this country, on methods for controlling such infections. Particular attention has been paid to borne infections and their control with the use of aviolet light and germicidal aerosols.

In 1939, the Preventive Medicine Committee of the Medical Research Council of Great Britain appointed the Subcommittee on Cross Infections in Hospital Wards. This committee* has just published an abbreviated report that contains practical suggestions for civilian hospitals in wartime Britain. It may well serve as a guide for use in hospitals everywhere, as well as for the planning of improvements in hospitals or in the construction of new hospitals during the postwar period.

In a foreword to this report, Sir W. Wilson Wilson, the British Minister of Health, points out the great and steady drain that cross infections make on hospital finances and efficiency. Overhead expenses continue and admissions are delayed while the wards are kept in quarantine. Patients who are detained on account of intercurrent diseases may even die and are, in any case, a continuing source of expense and anxiety. For these reasons, requests for improvements and equipment calculated to lessen the risk of such infections should receive careful attention. When new construction is contemplated, the prevention of cross infection should be an over-riding consideration, and expert advice should be sought.

The report outlines in adequate detail the sources and modes of infection, and indicates in a practical way how these actually come about in practice. Particular attention is called to the great increase in bacterial counts in the air of hospital wards during sweeping and bedmaking. The methods of preventing and controlling cross infection are given in considerable detail, including general administrative procedures, those for admitting patients and methods of isolation nursing. The problem of hemoprophylaxis is considered. The role of ward attendants and ways of minimizing infection from this

source, as well as from the medical and hospital personnel, are given appropriate attention.

Many forms of labor-saving devices are mentioned. Simple methods for the control of contact and mediate infection are enumerated. These include washing of the hands, care of laundry, preparation of food, proper care in taking temperatures and in the handling of children's playthings and a technic for surgical dressings. The problem of controlling droplet-borne and dust-borne infections is also considered from the point of view of ventilation, bed spacing and the use of face masks and aerial disinfectants. Methods are outlined for the treatment of bedclothes and that of ward floors with spindle oil or another suitable oil in such a manner as to reduce or to eliminate dust.

An entire section is devoted to the procedures to follow on the occurrence of cross infection in a ward. Detailed methods are given for discovering the source and the mode of spread, attention being given to individual diseases, such as hemolytic streptococcus infections, measles, enteric infections, chicken pox and gonococcal vulvovaginitis.

At the end of the memorandum is an appendix containing an outline of details concerning disinfection and sterilization. A second appendix gives practical rules for isolation nursing in cubicles or on open wards. Others outline special precautions for maternity units, rules for ward dressing teams and methods of applying dust-preventing oils. Finally, there is an appendix outlining a course of practical bacteriology for nurses, with suggestions for demonstrations and practical work for the instruction of all interested personnel in the part they must play in preventing cross infection.

All the subject matter outlined is contained in twenty-eight pages of text. Every physician and administrator who is responsible for the care of hospitalized patients can readily profit by reading and studying this brief memorandum. The details are also well adapted for use in the teaching of nurses in training schools. Furthermore, graduate nurses who are responsible for the care of patients in hospitals will profit by acquainting themselves with the contents of this memorandum.

**The Control of Cross Infection in Hospitals*. Memorandum prepared by the Committee on Preventive Medicine of the Medical Research Council the Sub-Committee on Cross Infections in Hospital Wards. Medical Research Council, War Memo. No. 11, 34 pp. London. His Majesty's Stationery Office, 1944.

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UNITED WAR FUND

Now in full swing, the Greater Boston United War Fund campaign reflects the will of a great community working together for the common good. Before Thanksgiving Eve, \$7,650,000 must be raised to meet the 1945 needs of home-front and fighting-front services.

Year in and year out, services here at home are adding new and tangible meaning to the words, "Life, Liberty and the Pursuit of Happiness." Throughout the world, the war services are giving convincing proof of their worth. United Nations Relief provides food, shelter and medical supplies to sixteen allied countries — Belgium, Great Britain,

Czechoslovakia, Denmark, France, Luxembourg, Greece, Italy, Lithuania, Norway, Holland, the Philippines, Poland, Russia, China and Yugoslavia. Refugee Relief Trustees helps refugees of war-torn countries until they become integrated and contributing members of a free society. The United States Committee for the Care of European Children brings youngsters to this country from ravaged countries and undertakes their care while they are here.

"Show That You Care" is this year's campaign cry. Physicians have always cared, serving rich and poor alike. And they, because they are physicians, understand better than others the harmful results of malnutrition in occupied countries and the deteriorating effect of the war prisoner's life. Knowing so well what is at stake, they should give generously and wear their Red Feathers with pride.

THE CONTROL OF CROSS INFECTIONS IN HOSPITALS

THE modern treatment of many severe diseases often requires elaborate methods of diagnosis and many forms of therapy, which are difficult to carry out in the home. Most hospitals are provided with the necessary facilities and with properly trained personnel for these diagnostic and therapeutic measures. The fact, however, that many people sick with various infectious diseases are brought together in the same wards and buildings carries with it the risk that patients will acquire infection that they did not have on admission and that they would not have acquired if treated at home. The greatest risk of cross infection is, of course, in infants' and children's wards, where sources of infection are always present. With adults, there is considerable risk for those with wounds and burns and for women in the puerperium.

The last decade has seen great advances in the study of such infections. The ability to identify specific types of pneumococci and streptococci has made possible the tracing of cross infections due to these organisms. More recently, extensive studies have been carried out, particularly in Great Britain

it is, does not begin to indicate the real reasons Doctor Breed's conspicuous success in the practice of medicine and in the art of living. His sincere unflagging interest in people, his patient understanding and his gift for friendship are attested to by a host of devoted patients and friends—these hardly be separated, since so many of his patients became his friends, and so many of his friends his patients. As the late Professor Hanser wrote of him in the autobiography *As I remember Him*, "... [he] was one of those precious individuals whom nature had meant to be physicians."

certain significant factors in his life cannot be dissociated from his complete personality: his devotion to his home and family, after those years when he had had so little of either; his love of music—he was once rated by Philip Hale as the amateur violinist in Boston; and his interest in fishing—he was a lover of little rivers and of lakes and ripples.

Let this be taken as a tribute to his particular genius, that to his friends he is still a present, a vibrant reality, to be found at the Tavern Club with his violin, or encountered in the corridors of the Massachusetts General Hospital, or met upon a rocky beach of Moosehead Lake. If remembrance of some part of immortality, then that part of mortality is assured.

"They have not gone, nor can they dwell apart
Who still hold place within some human heart."

J. G.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BLAISDELL—J. Harper Blaisdell, M.D., of Winchester, died October 25. He was in his fifty-ninth year.

Dr. Blaisdell received his degree from Harvard Medical School in 1911. He limited his practice to dermatology and fought for many years at the Harvard Medical School. He was a member of the staffs of the Massachusetts General Hospital and the Boston Dispensary and served as consulting dermatologist for several other hospitals. He was a member of the American Medical Association, the American Dermatological Association and the Atlantic Dermatological Conference. He was past president of the New England Dermatological Society and, at one time, chairman of the Section of Dermatology and Syphilis of the American Medical Association. He had long been prominent in the affairs of the Massachusetts Medical Society, and was one of the time movers in the organization and administration of the Blue Cross and the Blue Shield.

His widow and two sons survive.

CHRISTIERNIN—Charles L. Christiernin, M.D., of Maplewood, New Jersey, died October 18. He was in his sixty-seventh year.

Dr. Christiernin received his degree from Harvard Medical School in 1906. At the time of his death he was medical director of the Metropolitan Life Insurance Company of New York. He was active in the medical societies of the United States and Canada, and was well and favorably known in both life-insurance and health circles in the two countries. He had served as treasurer, vice-president and resident and as a member of the Executive Committee of the Association of Life Insurance Medical Directors. He was a member of the American Medical Association.

His widow and two sons survive.

FENWICK—George B. Fenwick, M.D., of Chelsea, died October 27. He was in his sixty-eighth year.

Dr. Fenwick received his degree from Harvard Medical School in 1904. He was a member of the local Selective Service board and had organized the medical unit of the Massachusetts Committee on Public Safety in Chelsea.

His widow, a daughter and a son survive.

MARSHALL—Commander John R. Marshall (MC), U.S.N.R., of Somerville, died October 14 at the United States Naval Hospital at Shoemaker, California, where he was stationed as a surgeon. He was in his fifty-seventh year.

Dr. Marshall received his degree from Harvard Medical School in 1918. He was a staff member of the Cambridge Hospital, the Symmes Arlington Hospital and the Lawrence Memorial Hospital and had formerly served at the Mayo Clinic. He was a member of the American Medical Association and a fellow of the American College of Surgeons.

His widow, a daughter and two sons survive.

SHAW—Albert J. Shaw, M.D., of Newton, died May 23. He was in his seventy-third year.

Dr. Shaw received his degree from Harvard Medical School in 1894. He was a member of the American Medical Association.

His widow survives.

SIMS—Frederick R. Sims, M.D., of Northampton, died October 26. He was in his sixty-sixth year.

Dr. Sims received his degree from Harvard Medical School in 1902. He served in the state hospitals at Danvers and at Taunton before going overseas as a major in the Medical Corps in World War I. He was chief medical officer at the Bedford Veterans Hospital from 1934 to 1937. At the time of his death he was psychiatrist and retired chief medical officer of the United States Veterans Administration Facility in Northampton. He was a member of the New England and the American psychiatric societies.

His widow, a son, a brother and a sister survive.

CORRESPONDENCE

DEPRIVATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held October 18, the Board voted to revoke the license of Dr. Robert E. Conlin, 18 Auburn Street, Woburn, to practice medicine because of gross misconduct in the practice of his profession as shown by his conviction in court and treatment of a patient.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

To the Editor: At a meeting of the Board of Registration in Medicine held October 18, the Board voted to revoke the license of Dr. Morris J. Kupper, 961 Blue Hill Avenue, Roxbury, to practice medicine because of gross misconduct in the practice of his profession as shown by collusion.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

TRANSFUSION ACCIDENTS

To the Editor: In the December 8, 1938, issue of the *Journal* you were kind enough to publish my letter concerning a series of severe transfusion accidents in all of which the patients had died following the administration of incompatible blood. Since then, it has been my misfortune to have seen an increasing number of similar cases. Although I have often commented on them both in writing and at lectures, it seems wise at this time to make the following suggestions:

Give whole blood only if it is *urgently* indicated, and not simply as a "boost" or because it is readily available from a blood bank. Too many transfusions, particularly now that blood banks have been established in a large number of hospitals, are being given as a more or less routine measure in surgical operations. Indications for the use of whole blood are relatively few.

OBITUARY

WILLIAM BRADLEY BREED
1893-1944

"When a man becomes dear to me,
I have touched the goal of fortune."

William Bradley Breed was born in Syracuse, New York, the younger son of a physician. He lost his father when a child, and after the death of the brother, his mother took him to Germany for a year, where he continued his education and studied the violin. He later graduated from the Hackley School in Tarrytown-on-the-Hudson. When he entered Harvard College in 1911, his mother established herself in Cambridge, remaining there until her death, while he was still an undergraduate.

During his college years he continued to show an interest in music; he was a member of the University Musical Clubs and leader of the University Mandolin Club. He had membership also in Delta Upsilon, the Speakers' Club and the Deutscher Verein. At the Harvard Medical School, from which he graduated with the class of 1919, he was a member of the Boylston Medical Society, Phi Rho Sigma, the Aesculapian Club and the Stork Club.

In 1918 and 1919 Doctor Breed served as medical intern in the Massachusetts General Hospital; the following year he held a residency at the New England Deaconess Hospital, later establishing himself in the practice of internal medicine in Boston.

He was married in 1925 to Ruth Williams, of Dedham, who survives him, with their three children, Elizabeth, Sylvia and William.

The posts that he occupied and the positions of trust that he held are ample evidence of the esteem

in which he was held by his professional colleagues. For the greater part of his active medical career he was on the staff of the Massachusetts General Hospital, receiving his final appointment as physician in 1936, the same year in which he became member of the General Executive Committee. In that year, also, he was appointed associate in medicine at the Harvard Medical School.

From 1925 until 1936 he was visiting physician

to the House of the Good Samaritan, joining its honorary staff in the latter year. He was physician at St. Luke's Hospital and a member of the staff by the courtesy of the New England Baptist, the New England Deaconess, the Faulkner and the Robert Breck Brigham hospitals. He became an associate editor of the *Journal*, then the *Boston Medical and Surgical Journal*, 1923, retiring from the less active editorial board in 1937. In 1942 he was appointed to the Committee on Publications of the Massachusetts Medical Society.

For a number of years Doctor Breed was a member of the Council of the Society, and in 1943 and 1944 he served as chairman of the

Participation Committee. He was a member of the New England Heart Association, the American Clinical and Climatological Society and the American College of Physicians. In the American College of Physicians he had been governor for Massachusetts since 1935 and chairman of the Board of Governors since 1942, also being a member of the Committee on Credentials and a member *ex officio* of the Board of Regents.

His published articles appeared in the *Boston Medical and Surgical Journal*, the *New England Journal of Medicine* and the *Annals of Internal Medicine*.

Such a list of positions held and of varied contributions to medical progress, however outstanding,



WILLIAM BRADLEY BREED

Bachrach

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POSTWAR PLANNING IN ANESTHESIOLOGY*

HENRY S. RUTH, M.D.†

PHILADELPHIA

ANESTHESIOLOGY has now established its unequivocal value to the surgical and medical professions, and to those seeking medical care coming under its jurisdiction. The inherent dynamic nature of the specialty with its present broad application was gaining momentum rapidly during the immediate prewar period. Its increasing sphere of application was being affected less and less in those years by specious economic opposition and examples of personal and institutional obstacles. A permanent retardation of its growth because of the temporary cessation of its activities in civilian life engendered during the war is therefore not expected. Conversely, growth may be further stimulated in the postwar period because of its wartime contributions and experiences. Thoughtful guidance and planning are indicated, however. The statements and proposals suggested here spring from an attempt to project into the future the trends exhibited by anesthesiology as observed during the past twenty years, coupled with the possible effects of the impact of a sudden peace following total war.

Postwar planning is a vitally important problem at this time. The details of proposals for the management of the initial peace period should, however, as yet remain flexible. This country has lived the period where the major issue of victory or defeat was not clear, but its people are still ignorant of the element of time required for victory, its ultimate cost from numerous angles and the sociologic conditions that will be present thereafter. Many authorities believe that postwar medical practices will undergo a metamorphosis of a type as yet undetermined. Some believe that the very structure of modern medicine may be altered. If such future attempts at outside control are successful, the younger specialties may be affected first. Those within the specialty should look forward to future progress for many reasons, one of which will be outlined, irrespective of possible future changes in medical practice. It is

believed, also, that there will be the continued active support of a growing portion of the medical profession in the future, as now.

The first problem of postwar medical planning naturally concerns the return to civil life of medical men in military service. For anesthesiology, these may be logically and conveniently grouped in three classifications. The first comprises the adequately trained, fully experienced anesthesiologists. Some members of this group were professors in universities and directors of anesthesia in large hospitals, in situations in which they could contribute to both instruction and medical service, according to their qualifications. Without doubt, the greater number of these positions will be awaiting the former incumbents on their return, to the mutual satisfaction of both institutions and teachers. A few may seek new positions for many reasons, and for these replacement will be indicated. A proposed plan for the relocation of these persons will be discussed.

When the present war began, the importance of anesthesiologists was recognized by the armed forces, and courses of instruction for medical officers in both military and civilian hospitals were initiated. In this way, material numbers of men received their basic training in anesthesia. It is the general belief that most of the officers so trained, who comprise the second group, will continue in the specialty after the war; for example, the majority of the men thus trained in Philadelphia expressed such a desire both during training and thereafter. A portion of these officers will have received sufficient additional training or supervised experiences to enable them to practice immediately on discharge. The same will be true of men who had just completed their formal training at the outbreak of the war and immediately entered the Service, with no opportunity for civil practice. This group will also desire aid in suitably locating themselves.

The third group is composed of men who require additional training. A portion of them will consist of those medical officers who were hurriedly and

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

†Professor of anesthesiology and head of the Section on Anesthesiology, Jefferson Medical College and Hospital

If, after due consideration, it is believed that whole blood and not plasma or fluids should be given, it is imperative:

To type both the patient and the donor with high-titer serums.

To retype banked donor blood before use even if it has already been labeled.

To cross match the donor's cells with the recipient's serum. This should be done by the Landsteiner-Levine test-tube technic, the slide cross-matching technic often being unreliable.

To have the results of the cross match checked either by an experienced technician or by an experienced physician. Reliance on inexperienced personnel for something as inherently important as a blood-grouping test may, and often does, result tragically. Unfortunately it appears to be a frequent practice to entrust blood-typing and cross-matching procedures to the lowliest intern or the newest technician.

If the above procedures have been carried out the transfusion may be started. During administration of the first 50 to 100 cc., the patient should be carefully observed by an experienced observer. Any complaint of pain in the flanks, of a sense of constriction in the chest or even of a "queer" feeling should be carefully heeded and the transfusion should be immediately stopped. This requires a wide-awake patient who can feel pain and other sensations and precludes the use of transfusions during both general and spinal anesthesia. If the first 50 to 100 cc. of blood go in without reaction, it is reasonably safe to assume that the blood is compatible and that the cross match has been satisfactorily performed. *This in vivo test is of utmost importance and should never be ignored.* It is often lifesaving, since the recipient can take perhaps up to 100 cc. of incompatible blood without too much difficulty, whereas more than that amount results in an irreversible agglutination of red cells within the circulation and the renal glomeruli and in the deposition of hematin plugs within the tubules. The end-results of such a severe reaction—aside from hemoglobinuria and hemolytic anemia—are renal failure, azotemia and almost always death. No amount of fluids, alkalies, hypertonic solutions and so forth can modify this essentially mechanical nephropathy, in which the glomeruli and tubules are largely blocked and functionless.

If the patient is pregnant or has been delivered, or if more than one transfusion is contemplated, an Rh determination should be performed in addition to the regular blood-grouping tests. If good anti-Rh testing serum is not available, an exceedingly careful cross match (test-tube technic) should be performed, and the in vivo reaction carefully watched.

As I have repeatedly stated, these severe transfusion reactions of incompatibility are by no means scarce. I have seen many of them, but few are reported. Their essential tragedy becomes greatly enhanced when it is realized, too late, that the transfusion was not essential and could well have been omitted.

The following conclusions may be made:

Too many transfusions of whole blood are being given, often without sufficient indication.

Typing and cross-matching procedures should at least be checked, if not completely performed, by thoroughly trained and competent personnel, using the best available methods.

Whole blood should not be given to a patient while under the influence of a general or spinal anesthetic.

The patient should be carefully watched during the administration of the first 50 to 100 cc. of blood, and the transfusion should be immediately discontinued in the presence of a reaction, however slight.

The severe transfusion reaction is best treated by its prevention.

Prevention may be facilitated by standardization of technic, methods of administration and so forth. This might well be placed under the purview of a committee of the Massachusetts Medical Society.

WILLIAM DAMESHEK, M.D.

NOTICES

HARVARD MEDICAL SOCIETY

It has been decided to renew the meetings of the Harvard Medical Society, which were discontinued at the beginning of the war. The first meeting will be held at 8:15 November 14, in the Amphitheater of the Peter Bent Brigham Hospital. Subsequent meetings are scheduled for the Tuesday evening of each month. Each meeting will with the presentation of a clinical case with discussion followed by three papers of fifteen minutes' duration and a five-minute discussion of each paper. Arrangements have been made for the publication of reports of these meetings in the *Journal*.

Under this plan it will be possible to present clinical studies as well as the results of fundamental investigations. This should afford an opportunity for the student, the faculty and the interested medical profession to be in touch with the many studies now being carried on in different departments of the Harvard Medical School and its associated teaching hospitals.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

A meeting of the New England Ophthalmological Society will be held at the Massachusetts Eye and Ear Infirmary 243 Charles Street, Boston, on Tuesday, November 14, at 8 p.m.

Following the business meeting, Miss Anita B. L. Giaracine will speak on the topic "Bacteriological Observations." A symposium "Some Nonsyphilitic Interstitial Lesions of the Cornea" will then be presented by Drs. C. Verhoeff, Lahey and Cogan. This will be followed by a "Preliminary Report on Bilateral Surgery in Alternating Strabismus" by Drs. Lemoine and Moore, and Miss Alice S.

SUFFOLK DISTRICT MEDICAL SOCIETY

The fall dinner of the Suffolk District Medical Society will be held on Saturday, November 18, at the Harvard Club of Boston, 374 Commonwealth Avenue, Boston. A session beginning at 6:00 p.m. will be followed by dinner at Harvard Hall at 7:15. His Excellency, Leverett Saltonstall, will speak on the topic, "Medical Social Security and Dr. Roger I. Lee on 'Health Insurance?'"

It is urged that doctors bring their wives and particularly that the wives of all doctors absent in the service, who are not the doctor is a member of Suffolk Society, be invited by members as their guests. Each member who sends the treasurer with his own application the names of service wives will receive free tickets for them. The tickets \$3.00 each, must be purchased in advance by sending a check to the treasurer, Dr. Richard S. Eustis, 319 L Street, Wood Avenue, Boston 15. Other members of the Massachusetts Medical Society may apply after November 8.

UROLOGY AWARD

The American Urological Association offers an award "not to exceed \$500" for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merit of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write to the secretary for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming June meeting of the American Urological Association.

Essays must be in the hands of the secretary, Dr. Theodor D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before March 15, 1945.

one physician anesthetist, and that it would require many years to change over to the status in which all anesthetics would be administered by physicians, even though such a thought might be accepted. On the other hand, it is also true that there are many large hospitals that could utilize the services of a number of physician anesthetists. I believe that a hospital of 125 to 150 beds can support adequately one anesthesiologist, with 100 per cent of his time devoted to anesthesiology.

It is not unlikely that experiences encountered during the present war will greatly increase the opportunity for anesthesiology. Before the war, large numbers of surgeons had never had the experience of operating under conditions provided by the physician anesthetist. Many of them had never attempted to acquire the services of a physician for anesthesia. They could, therefore, through personal experience, have no basis for a comparison of the operating conditions provided by the two types. Many of these surgeons have made or will make their first contacts with competent anesthesiologists in the armed forces and work under the improved conditions provided by them. After such an experience, it is to be seriously doubted whether many of them will be content on their return to civilian practice to retrogress to the inferior type of unsupervised technician anesthesia, where, as the law requires, they must assume full responsibility for the anesthesia, even though fully occupied with the technical requirements of the surgery, and at the same time must dictate treatment and supportive measures during the operative period. On the other hand, there will be numerous surgeons who have long been accustomed to the advantages provided by anesthesiologists who will be exposed to the nonprofessional type of service. It may be assumed that a large portion of this latter group will become even more active in furthering the advance of anesthesiology after the war.

From the viewpoint of war itself, facilities for the training of anesthesiologists should be enlarged. Disturbing though it may be, the possibility of a third world war has already been discussed by reputable international authorities. With this thought in mind, plans should now be laid in order that greater numbers of anesthesiologists may be available than existed at the outbreak of World War II. Recent experiences in the combat areas have indicated that the presence of qualified anesthesiologists at the immediate front under actual fire is quite valuable. Nurses cannot be assigned to such duties, and at the present time there are not sufficient numbers of experienced physicians for this purpose.

Some hospitals, because of the shortage of technician anesthetists, have attempted to locate physician anesthetists during this war period. They quickly learned that the shortage of physicians is more acute than that of technicians. In the post-

war period, these same hospitals should be stimulated to seek again the services of physicians. By doing so, they could probably avoid future inadequate anesthesia service. An example may be cited by comparing two large general hospitals in the same city. Hospital A for many years has had physician anesthetists, and, for the last fifteen years, residents in training. Hospital B formerly had only technicians, and placed a qualified anesthesiologist in charge only after the war had begun. Hospital A, although contributing its comparative share of personnel to the war effort, has so far provided adequate anesthesiologic care, partly because physicians usually consent to work longer hours. Also, more work has been placed on the older staff members. Although reduced 50 per cent in number of residents by the Procurement and Assignment Service, it was able to attract some of the military unit as assistants because it was well established as a training center. Hospital B, with no residents as a standard practice, could, of course, obtain no resident in anesthesiology under Procurement and Assignment Service. A large number of technicians were sent to the armed forces, and because their number could not be expanded, it became necessary to rely on interns with no experience in anesthesia. Since it is impossible for the single anesthesiologist to supervise all the work, the anesthesia service has been markedly impaired. If Hospital B had initiated this service in the prewar period, the Procurement and Assignment Service would have allowed it 50 per cent of its former residents under the 9-9-9 program and the remaining physicians would have worked longer hours with the result that the hospital would have been able to supply its share of trained men for the armed forces and that the civilian population patronizing the hospital would not have suffered anesthesia service of lowered quality.

This discussion will be concluded by a consideration of the economics of the specialty. The transition from fees collected by the hospital for the services of a technician with a short and inexpensive period of training to that of a fair fee for a physician commensurate with his ability and prolonged and expensive training is a difficult one. Attempts have been and will continue to be made to enlist the services of physician anesthetists at full-time salaries at a level only slightly above that allotted for technicians. A great error will be committed if the medical profession allows these attempts to be successful. It is only just that a physician should expect recompense commensurate with his ability and intelligence, his training and the value of service rendered. If anesthesiologists cannot expect a financial return comparable to other specialties, the desirable type of young physician will little desire to enter or remain in the field. It is here, also, that practitioners of the surgical specialties can contribute wisely by their support. It has been

incompletely trained for the emergency and were able to provide the needed service in the combat forces, but because of the incomplete nature of their preparation should be discouraged from entering civilian practice without completing their formal training. Plans should be made for sufficient suitable residencies to provide this training. The same is true of those whose interest in anesthesia has been stimulated for the first time by the war, either by observing the efficient application of modern anesthetic practices or witnessing at first hand the effects of its mismanagement in remote corners of the world, or through recognition of the opportunities offered to young physicians by the practice of anesthesiology.

It appears that some medium should be set up for the collection and filing of data concerning opportunities for the returning qualified anesthesiologists.¹ It may be that the American Society of Anesthetists might best serve this purpose. Dr. Paul M. Wood, of New York City, the present chairman of the Professional Relations Committee of the society, has stated that his committee is willing to serve in this capacity. Institutions desiring to establish contact with qualified physicians could file their specific requirements, the opportunities for service offered and the economic features, together with other essential information, with this committee. Discharged officers would then have these data available and be able to locate themselves easily and satisfactorily, with little lost time and effort.

For officers requiring graduate study in anesthesiology, additional training facilities should be provided through increasing the number of available residencies. According to the most recent published statistics, only forty-three vacancies are now offered by existing approved residencies, assistant residencies and fellowships for this type of training.² It has been estimated that should the war end by 1945, as many as 20,000 physicians will be released from military service who have never had the opportunity of beginning the private practice of medicine.³ So many will seek residencies that it is believed that 13,000 residencies will be required, whereas only 5500 are available under normal conditions.⁴ By these figures, some idea is conveyed of the proportionate increase of residencies in anesthesiology that may be required.

It seems that the postwar period would be an appropriate time to stimulate training facilities not only in quantity but also in quality. The selection of men for training should be carried out with great care. Since the specialty has expanded its activities, the mental requirements for its application have likewise increased. Residencies that are set up for the mere purpose of providing clinical anesthesia for surgical patients with unqualified or no supervision must be discontinued. A definite plan of instruction in charge of capable

physicians is necessary, and this plan must be summated efficiently. The clinical work should be under constant adequate supervision. Clinical training should include instruction and experience in all types and methods of anesthesia. The days are past when a physician could call himself anesthesiologist only because of his ability with inhalation agents and technics. It is true that thorough knowledge of physiology, pharmacology and other basic sciences is required to administer anesthetic agents by inhalation technics with greatest safety and efficiency, but spinal, intravenous and regional technics are too valuable to be lightly treated or ignored. Gas therapy, for example, the correct administration of oxygen and helium, — diagnostic, prognostic and therapeutic nerve blocks and resuscitative procedures are important aspects of training. Training in bronchoscopic technic for postoperative aspiration of air passages is quite valuable. In some institutions the management and direction of blood and plasma banks and transfusions are demanded of the anesthesiologist. Unless the above aspects of anesthesiology are included, residencies in anesthesiology can be made a mere sham for the economic well-being of the institution where they are offered.

From recent personal experience in Philadelphia, I believe that the exchange of senior residents between institutions offering training is invaluable from all aspects. In addition to broadening the experiences of the residents, it facilitates exchange of ideas, and frequently offers training in aspects of the field not emphasized at the institution where the bulk of instruction and training has been taken. In time, with the establishment of comprehensive foreign residencies, exchange with residents of other countries does not appear to be impossible.

It appears unlikely that the saturation point of trained anesthesiologists will be reached for a long time. Whereas many other specialties are overcrowded, the reverse is true in anesthesiology. There are few undeveloped locales for its application to the number of trained personnel now available and to be supplied by those returning from the armed forces. This is impressive. Less than 250 anesthesiologists have been certified by the American Board of Anesthesiology. The membership of the American Society of Anesthetists is approximately 1500. On the other hand, over 7500 hospitals are listed by the American Medical Association either as being approved for internships, residencies, and fellowships or as measuring up to the standards set forth by its Council on Medical Education and Hospitals. This shows a ratio of five hospitals to one practicing anesthesiologist. Few specialties are able to show the numerical possibilities of such a ratio for every physician majoring in that field and at the same time to offer the same opportunity for as broad an application of it as does anesthesiology. It is gratifying to think that each hospital would not be capable of supplying

CASE REPORTS

CASE 1. J. M., a 38-year-old Scottish bus driver, was admitted to the hospital in great respiratory distress that was the culmination of 6 years' progressive diminution of exercise tolerance. The respiratory history included four or five episodes of pneumonia, three of these in the first 3 years of life, and frequent milder upper respiratory infections interposed. For 6 years the patient had been coughing up as much as a half cupful of yellowish-white sputum a day. For 4 years his exercise tolerance had been almost nil. There had been episodes of dyspnea at night with cough. He had spent the 4 weeks previous to admission sitting in a chair in more or less continuous respiratory distress.

Physical examination revealed an undernourished, middle-aged orthopneic man breathing with prolonged expiratory and inspiratory effort. The accessory muscles of respiration were extensively called into play, the shoulder girdles being fixed by grasping the bed or arms of the chair with both hands. There was infrequent nonproductive cough and marked cyanosis. The chest was strikingly emphysematous in appearance and hyper-resonant, with diminished tactile fremitus, distant breath sounds, a few scattered crackling rales but no rhonchi. The lower extremities were cold and blue, with soft pitting edema of the feet; circulatory studies established this edema as due to dependency of the legs during the 4 weeks of sitting and not to cardiac disease or cardiac failure. Chest films revealed marked emphysema of the lower lobes of the lung, whereas a review of lipiodol studies made 2 years previously showed bronchial irregularities of the type frequently seen in asthma and chronic bronchitis rather than true bronchiectasis. There was a polycythemia with a hemoglobin of 20 per cent and a red-cell count of 6,300,000; the white-cell count was 12,000, with 73 per cent neutrophils and no eosinophils.

After 9 days' stay in the hospital, during which many forms of medication were exhibited, including ephedrine, aminophyllin and adrenalin, the patient returned home essentially unimproved. One week later he was readmitted in worse respiratory difficulty than before, with cough, productive of thick, yellowish-white sputum, and a low-grade elevation of temperature, both of which rapidly subsided. He was more cyanotic, anxious and apprehensive than previously and was often mentally dull and disoriented. The chest, which showed some medium rales on admission, became completely silent within 48 hours, without change in the characteristics of the respiration. That there was no significant cardiac factor was indicated by a normal ptoic heart, an electrocardiogram within normal limits, a circulation time (Decholin) of 15 seconds (normal) and a venous pressure of 35 mm. of water (low normal). The vital capacity on repeated measurement over a period of days was 1000 cc. The arterial blood taken at a time when the patient's condition was stationary but somewhat improved over what it had been at the time of admission showed an arterial oxygen saturation of only 60 per cent (normal, 95 per cent).

CASE 2. W. D., a 64-year-old ex-salesman, was admitted with the chief complaint of marked shortness of breath on exertion and chronic productive cough, both of 6 years' progression. There was a long history of repeated respiratory infection, beginning with influenza in 1918 and including two episodes of extreme dyspnea of an hour or more in duration, precipitated by walking unusually far and characterized by paroxysmal cough and orthopnea. The admission was precipitated by a "cold" 2 weeks previously, subsequent to which the exercise tolerance was limited to walking 25 yards slowly on the level.

Physical examination showed a pale, undernourished man with somewhat labored respirations and a cyanotic hue of the lips and nail beds. Respiration involved abnormal muscular effort and showed prolongation of the expiratory phase; on deep inspiration the costal margins moved inward. The chest was hyper-resonant, with diminished cardiac dullness and a low diaphragm showing very poor excursion. The breath sounds were faint, with a prolonged expiratory phase and occasional basal rales. A few scattered sibilant inspiratory and expiratory rhonchi were noted on admission, but within 2 or 3 days these adventitious sounds were no longer heard, although there was no marked symptomatic improvement.

X-ray examination showed marked emphysema of the lungs, with a low diaphragm having less than 1 cm. excursion, and a normal ptoic heart. Lipiodol injection of the left lower

main bronchus showed no true bronchiectasis but square endings and minor irregularities in diameter of the bronchioles, "such as is commonly found in asthma and emphysema." A normal electrocardiogram and a circulation time (Decholin) of 16 seconds (normal) supported the x-ray and clinical evidence of cardiac normalcy.

The vital capacity was consistently 1800 cc. The arterial oxygen saturation was 87 per cent (normal, 95 per cent). The carbon dioxide combining power of the plasma was 77 vol. per cent (normal, 50 to 70 vol. per cent). Marked dyspnea resulted from walking slowly 100 feet on the level.

CASE 3. H. H., a 51-year-old shoe cutter, was admitted with the complaint of progressive "shortness of wind" of 10 years' duration. He had been an unusually fine athlete, indulging competitively in running, jumping, boxing, wrestling and various other sports up to the age of 40 years, at which time he was still able to outdistance younger men in 100-yard and 200-yard sprints. During the subsequent 5 to 6 years, he cleaned hen houses on one day a week, with severe choking up from the dust and with cough and mucoid sputum for 2 or 3 days each time. During this period he began for the first time to notice unusual exertional dyspnea, which became progressively more marked, so that at the time of admission he was comfortable at rest but became markedly dyspneic on walking 50 yards at ordinary speed on the level, and after a much shorter distance when the weather was extremely cold. The only respiratory infective history elicited was that of "pneumonia" with hemoptysis after a thoracic injury at the age of 14, morning cough productive of thick yellow sputum for 7 years previous to admission and "influenza" with equivocal hemoptysis 8 months previous to admission.

Physical examination revealed a rather thin, well-developed, relatively young-looking man. The thorax was moderately emphysematous in appearance with an increased anteroposterior diameter, and there was loss of cardiac dullness and a low diaphragm of subnormal excursion. The breath sounds were distant, and there were fine to medium rales in both lung bases but no rhonchi. Chest films revealed marked emphysema, particularly in the lung bases. Lipiodol instilled into the right bronchial tree showed multiple diffuse areas of bronchiectasis in the right base anteriorly, the bronchi near the hilum appearing to be normal. There was a mild polycythemia, with the red-cell count 5,600,000, the hemoglobin 16.6 gm. and the hematocrit 49 per cent; the white-cell count was 7900, with 73 per cent neutrophils, 24 per cent lymphocytes and 3 per cent monocytes. There was no cardiac enlargement. The electrocardiogram showed slight right-axis deviation but was within the limits of normal. The circulation time (Decholin) was 13 seconds (normal).

The vital capacity, to the amazement of many, was consistently 4200 cc. The oxygen saturation of the arterial blood was 89 per cent (normal, 95 per cent).

* * *

It is at once evident that these 3 cases, which have in common extreme restriction in exercise tolerance, vary markedly in history and in various physical factors. J. M. (Case 1), with a vital capacity of 1000 cc. and an arterial oxygen saturation of 60 per cent, was orthopneic, but not extremely so when not excited. W. D. (Case 2), with a vital capacity of only 1800 cc. and an arterial oxygen saturation of 87 per cent, was not much more restricted in activity than was H. H. (Case 3), who had a vital capacity of 4200 cc. and an oxygen saturation of 89 per cent.

VITAL CAPACITY IN EMPHYSEMA

In considering Cases 2 and 3, with vital capacities of 1800 cc. and 4200 cc., respectively, yet similarly restricted exercise tolerance, one might conclude at first glance that the patient in Case 3 must have had a much greater impermeability of the respiratory

stated⁵ that good anesthesia costs more than poor or mediocre anesthesia, but a hospital acquiring the advantages of the modern developments in anesthesia will very soon appreciate that it has been more than repaid for the investment in terms of the patient's satisfaction, mortality and morbidity and the comfort of conscience. It has been estimated that on the average the financial return of the physician anesthetist could be made quite satisfactory by an increase in cost to the patient of only 5 per cent or less of the cost of the *entire* surgical venture, when compared with the cost of similar services by technicians.⁶ Few patients with any degree of intelligence would object to this small increase in expenditure if the benefits to be derived were explained to them, preferably by the surgeon. One effective method of management in this aspect that has come to my notice is for the surgeon to adopt the attitude before the patient that he believes his patients engage him because of his skill, and that it is therefore logical that he engage an anesthetist whose ability in anesthesiology is comparable to his in the field of surgery.

* * *

To summarize, postwar planning in anesthesiology should include first an agency or committee to

accumulate data on positions for trained anesthesiologists and for residencies available to officers requiring additional training when discharged from military duty. A greater number of residencies should be set up now, to begin functioning at the conclusion of the war. The standards of resident training should in no way be lowered. Institutions now without anesthesiologic services should be stimulated to plan for them in order to provide opportunities for those already trained and to be available in the future for those as yet untrained. If the medical profession in general will stimulate externally the natural inherent tendency within the specialty toward expansion, its accomplishment will serve as another example that the practice of medicine is not deserving of the attempted onslaughts on its present structure.

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THE ABNORMAL PHYSIOLOGY OF CHRONIC PULMONARY EMPHYSEMA*

Three Contrasting Illustrative Cases

ALFRED F. GOGGIO, M.D.†

BOSTON

IN RECENT years there has been a change in emphasis in the concept of the pathologic physiology of emphysema. To previous ideas concerning the diminution of pulmonary respiratory surfaces due to changes in the alveoli, the loss of capillaries and an increased diffusion coefficient for the blood gases has been added enlightening information about sundry mechanical inefficiencies of pulmonary ventilation. So much excellent work on normal and abnormal respiratory function has been done by Christie,¹⁻⁴ Alexander and Kountz,⁵⁻⁷ Barach,⁸⁻¹⁰ Hurtado,^{11,12} Hermannsen,¹³ Anthony,¹⁴ Knipping,¹⁵ Cournand¹⁶⁻²⁰ and others that it would be impossible to cover the material even in brief in a short space. Furthermore, the present interest in problems of high-altitude aviation has greatly enlarged the appreciation of pulmonocirculatory function and dysfunction and of the usefulness of oxygen in a variety of conditions. It is interesting to realize that in emphysema one has in some degree patients who live at "high altitudes" at sea level.

Clinically the term "pulmonary emphysema" is

*From the Medical Clinic, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School.

†Formerly, research fellow in medicine, Harvard Medical School

used without sufficient discrimination to include two fairly distinct etiologic types. One of these is the so-called "postural" or "senile" emphysema, which is the more frequent of the two but is relatively seldom of great clinical significance. The more significant type, variously named "chronic hypertrophic" or "obstructive" emphysema, has a somewhat younger age incidence and the etiologic factor of obstruction to breathing is usually fairly prominent on careful inquiry. Christie,⁴ who has done a great deal of valuable work in human emphysema, states that in his experience more than 90 per cent of patients with chronic hypertrophic emphysema give a significant history of asthma and chronic bronchitis. Experimentally, a pathologic lung picture similar to that found in human emphysema of this type has been produced in animals by various methods that produce chronic respiratory obstruction.²¹ It is intended here to present briefly 3 contrasting cases of chronic hypertrophic emphysema that illustrate several illuminating but frequently overlooked aspects of the disease, together with some unusual observations on the physiologic abnormalities that exist.

thus increasing the intrabronchial pressure as the patients do spontaneously, has been pointed out by Barach.⁹ It seems reasonable to suppose, then, that deep breathing exercises should be of use in limbering up the costovertebral articulations, which tend to become fixed, thus making thoracic respiratory movements easier. In Case 1 physiotherapy appeared to be beneficial.

SUMMARY

Three contrasting cases of emphysema are presented that illustrate many features of the disease. The usual method of measuring vital capacity is shown to be misleading owing to its neglect of the thoracic factor. By kymographic vital-capacity recording, the finding of severe limitation of exercise tolerance in the presence of a vital capacity of 4200 cc. is explained.

The importance of the bronchial obstructive element, when present, is stressed. The fact that marked bronchospasm may exist in the absence of adventitious sounds in the chest adds to the importance of the adrenalin test. The value of adrenalin therapy as an inhaled nebula or as adrenalin in solution by injection is emphasized. An objective test of efficiency should be made in each case.

Studies of the arterial blood and alveolar air in these and similar cases are the basis for discussion of the physiologic abnormalities that exist in this disease. These patients to some extent live at "high altitudes" at sea level. The anoxia that is found could be recognized as the cause of many symptoms in severe cases. Oxygen therapy is of value in preventing or breaking the vicious cycle of chronic anoxia, embarrassment of physiologic functions and respiratory fatigue, with resultant increase in general well-being and in exercise tolerance. Discontinuation of oxygen therapy over a long period of time in the same is neither so difficult nor so costly as is generally believed and may be of utmost value.

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be both nervous and chemical and may include afferent nervous stimuli from the active muscles, nervous stimuli from the higher centers, an abnormal rise in blood lactic acid and a change in the pH of the blood. Any increase in pulmonary ventilation, due to abnormal mechanical factors, can be accomplished only by great respiratory effort and to a very limited extent. Hence arise the limitation of exercise tolerance and the symptom of dyspnea.

TREATMENT OF EMPHYSEMA

In a disease such as emphysema in which cure is impossible and therapy so limited, the importance of utilizing measures that produce even very minor benefit is obvious. These measures will now be discussed.

Relief of Bronchial Obstructive Factors

That patients with emphysema are not infrequently benefited by bronchodilator drugs has been noted by many observers^{6,10} and has been illustrated in the cases here presented. The introduction of inhalation bronchodilator therapy by Lageder,²⁵ Graeser^{26,27} and others was an important advance in the treatment not only of asthma but also of emphysema. Barach and his co-workers⁸⁻¹⁰ have devised continuous vaporization methods, positive-pressure respiration and other measures of value in the treatment of these diseases. Of the many drugs credited with bronchodilator effect, the most generally effective is probably adrenalin; closely related drugs and ephedrine are also useful.¹⁰ The desirability of any such form of bronchodilator therapy should be objectively tested in each case of emphysema by observing its effect on the maximum voluntary ventilation rate, the vital-capacity exhalation-time curve or the vital capacity (a much less significant measurement).

Oxygen Therapy

The advisability of oxygen therapy in Case 1, in spite of the pronounced anoxemia and marked anoxic symptoms, was questioned by some on the ground that it might prove impossible to discontinue such therapy again in such a severe and chronic illness. Oxygen therapy was instituted in this case discontinuously, using a B.L.B. oronasal mask at flow rates of 3.5 to 4.5 liters a minute in such a way as to ensure more adequate sleep, relief from continual respiratory distress and improvement in general well-being. It was found that a nasal mask that allowed the patient to receive oxygen while eating was valuable in preventing the usual rapid loss of appetite and nausea that otherwise occurred at mealtime. The complete effectiveness of such therapy in returning the arterial oxygen saturation to normal is shown in Table 4. With the combined use of oxygen and adrenalin nebula such improve-

ment occurred in the patient's physical and physiologic condition that at the time of discharge from hospital his arterial oxygen saturation was 85 per cent.

Owing in part to the patient's indiscretions at home, it was soon found that oxygen would have to

TABLE 4. *Effect of Oxygen Therapy on the Oxygen Status of the Blood in Case 1.*

CONDITION	OXYGEN SATURATION	
	ARTERIAL BLOOD	VENOUS BLOOD
	%	%
Before oxygen therapy*	60.1	11.0
During oxygen therapy, at rest	96.6	65.0
During oxygen therapy, with mild exercise	98.7	—
After oxygen therapy (30 min. later)	71.7	46.5

*Done on a different day from the other measurements.

be made available in addition to the adrenalin and supportive medication that had been given. Arrangements were made with a commercial concern to keep the patient supplied with oxygen cylinders. The large cylinders of oxygen were delivered as required and connected for use at a cost of \$3.06 per cylinder; the patient was supplied with an oronasal mask, reducing valve and flow meter at a total cost of \$42 and instructed to use the oxygen sparingly but in such a way as to avoid excessive respiratory fatigue and to ensure adequate sleep at least every other night. He and his wife were thoroughly instructed in oxygen hazards. Follow-up at intervals of six weeks for a period of ten months showed a slowly progressive improvement in the patient's condition. His supplementary oxygen requirements dwindled from two and a half or three cylinders a week to one cylinder in two weeks. Adrenalin continued to be effective. At the time of the last visit the patient seemed to have much more energy than at any time previously. He could go up and down stairs for the first time in more than a year and could walk short distances each day. His color remained good, and his chest clear, and his ankle were free of edema. This therapeutic result was gratifying in view of the extremely grave prognosis at the time of admission to the hospital. This case seemed to illustrate forcibly the fact that in severe chronic pulmonary emphysema, if the vicious circle of respiratory fatigue, chronic anoxia, embarrassment of physiologic functions and general debility is broken, considerable improvement may be expected and maintained.

Abdominal Belts and Other Therapeutic Measures

In milder cases of emphysema and as supplementary measures in the severer cases, efforts to increase the mechanical efficiency of respiration by the use of abdominal belts of various types are reported by some to be attended by considerable success.^{6,28} Our experience with them has not been sufficiently extensive to warrant any definite statement. The value of exhaling between closed lip

overlying shadows and possibly to the minimal amount of calcium present in these small calculi. It has been suggested that an x-ray photograph taken in the oblique position is ideal for delineating calculi, since it eliminates the overlying obscuring shadows.¹

Although in Nicolas's² case the duodenal hemorrhage was due to erosion of a blood vessel by abscess formation, in the present case a calculus mechanically eroded the blood vessel just as it had worked its way through the wall of the duodenum. There have been cases reported in which the calculi have

pancreatic lithiasis there may have been previous subclinical attacks of acute pancreatic necrosis, with resultant calcium deposition, which may serve as a focus or foci of further calcification and resultant formation of calculi.

The history of alcoholism appears to be of significance inasmuch as a review of the literature shows an association of this finding much more frequent than can be explained by pure chance. It is possible that a combination of several factors produces the above condition. Thus, at times stasis with regurgitation of bile due to gastrointestinal upset caused by

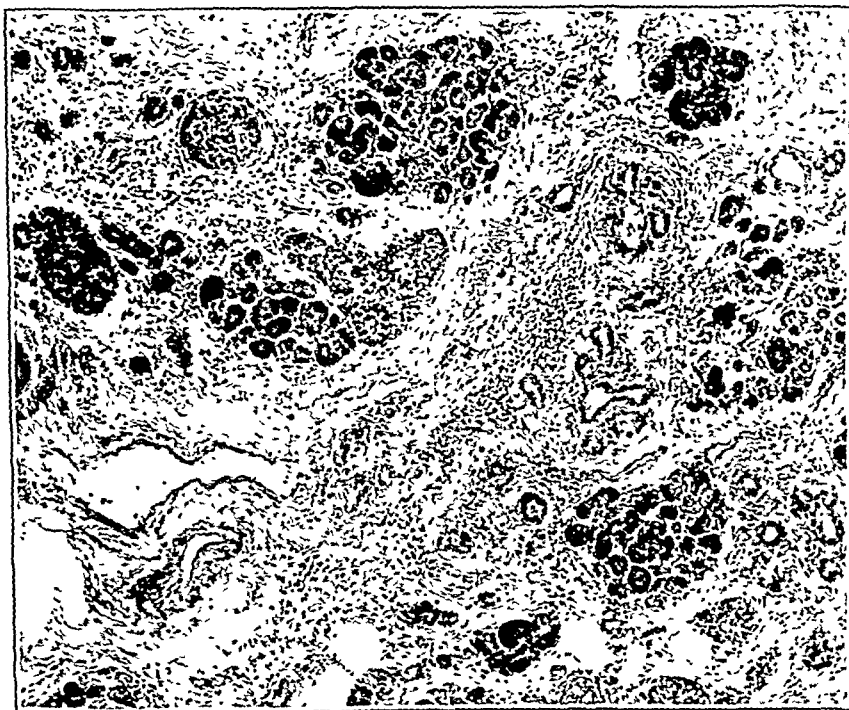


FIGURE 2. Photomicrograph of the Pancreas ($\times 35$).

Note the marked fibrosis, the diminution in number of acini, the lymphocytic infiltration and the dilatation of the ducts.

ruptured into the abdominal cavity, and similarly one in which a fistulous tract was formed, extending from the pancreas to the umbilicus, with discharge of pancreatic calculi onto the skin surface.³

Thus, although the mechanism of hemorrhage as a complication seems understandable, the etiology of pancreatic calculi is extremely difficult to explain and has been the subject of numerous theories, none of which have been proved. It has been suggested that the stasis of pancreatic secretion is the causative factor, yet experimentally both pancreatic ducts in animals have been ligated without production of calculi. It has also been claimed that the backflow of bile into the pancreatic ducts may, by its irritative action, lead to calculus formation. Experiments in which bile was introduced into the main pancreatic duct, however, similarly failed to produce the lesion. Pasternack⁴ has suggested that in cases of

alcoholism may initiate a chronic inflammatory reaction in the ducts, and calcium deposition then results, with the formation of calcium phosphate or carbonate stones. This may explain the presence of calcium, for although calcium is not a normal constituent of pancreatic secretion, it may be deposited in chronic inflammation.

In most cases of pancreatic lithiasis the ducts contain stones of varying size. These range from small gravel-like concretions to large stones, one having been reported as weighing 60 gm.⁵ They vary in color from grayish white to yellowish brown, depending on their admixture with organic matter, and their consistence is determined by their calcium content. The walls of the ducts are usually thickened by a fibrotic reaction and are often rigid owing to calcium deposition. The ducts vary in caliber, tending to be dilated, and are tortuous, with oc-

PANCREATIC LITHIASIS WITH ASSOCIATED INTESTINAL HEMORRHAGE*

Report of a Case

HERBERT FANGER, M.D.†

SALEM, MASSACHUSETTS

PANCREATIC lithiasis is not so unusual a clinical and pathologic entity as was originally believed.¹ The complication of fatal intestinal hemorrhage, however, is distinctly infrequent, only 3 cases having been reported in the available literature.^{2,3} Therefore, the following case seems worth while presenting.

CASE REPORT

A. C., a 63-year-old man, had been treated 3 years previous to admission for a "fatty liver" ascribed to alcoholism. He was given a high-caloric diet and high vitamin intake and appeared to recover from this episode. He remained in relatively good health until 1 year before admission, at which time he began to suffer from diffuse, poorly localized abdominal pain that was intermittent. No radiation of this pain was noted, nor was there any back pain. During that period, there were alternating bouts of constipation and diarrhea of increasing severity. In the 6 months before hospitalization, the patient noted occasional tarry or blood-streaked stools. His appetite diminished and he experienced easy fatigability. There was a 20-pound weight loss in 1 year. Two days before entry he had a severe attack of diarrhea, the stools being bright red. On entry he was quite weak and dyspneic on exertion.

Physical examination was not remarkable. The outstanding finding was marked pallor of the skin. Examination of the abdomen was negative.

Throughout the hospitalization, the patient had multiple episodes of bleeding into the bowel, as evidenced by tarry stools and at times by bright-red fluid blood. The bleeding time, coagulation time, clot-retraction time, prothrombin time and platelet counts were within normal limits. A brom-sulfalein function test of the liver was normal. Repeated barium enemas as well as x-ray examination of the gastrointestinal tract were not considered to be diagnostic. Sigmoidoscopy revealed fluid blood trickling down into sight, but no masses or other specific lesions could be made out.

Whereas usually the stools were positive for bile, for a period of 5 days there were clay-colored stools with no bile demonstrable. Urine examinations were at all times negative, no sugar being present.

In spite of repeated transfusions, the patient was considered a poor operative risk, and expired before a planned exploratory laparotomy could be performed.

Autopsy. The autopsy was limited to the abdomen. The major pathology was found in the second part of the duodenum. Just medial to the ampulla of Vater and at a slightly higher level there was an ulceration of the mucosa 4 mm. in diameter, from which protruded a fresh, friable blood clot. On its removal there was seen at the base of the ulceration a brownish-white, mulberry-shaped stone 3 mm. in diameter impinging on a small eroded blood vessel, the apparent source of hemorrhage (Fig. 1). On careful dissection, the ulceration was seen to represent the orifice of a sinus tract that, when traced into the pancreas, terminated in the duct formed by the union of the two major pancreatic ducts. This sinus tract was apparently formed by the inflammatory reaction evoked by the pancreatic calculi, which had caused erosion of the duodenal wall. Throughout the length of the pancreatic ducts there were numerous grayish-white, friable, granular calculi varying in size from tiny particles to masses 3 mm. in diameter. The ducts were markedly dilated, there being a cystlike dilatation just proximal to the ulceration through the duodenal wall. The margins of the dilated ducts were roughened and there was a definite fibrosis of the walls. The surrounding parenchyma showed a diffuse fibrosis with

many small foci of calcification, possibly representing gravel in the small ducts.

The common bile duct was distended in its distal third but no obstruction was demonstrable. The gall bladder was of normal size and free of calculi. The liver was enlarged and tawny yellow, and on section presented a slightly yellow



FIGURE 1. Photograph of the Ulceration in the Duodenum with the Pancreatic Calculus at Its Base (x2).

The probe is in the ampulla of Vater.

surface. The remainder of the abdominal examination was not remarkable except for the presence of blood in the stomach and intestines.

The significant findings on microscopic examination were confined to the pancreas and liver. The pancreas revealed dilated ducts containing cellular debris. There was a marked interlobular and intralobular fibrosis, with infiltration by lymphocytes and macrophages and a reduction in the number of acini. The islets of Langerhans were uninvolved (Fig. 2). The liver showed marked fatty infiltration of the hepatic parenchyma.

The pathologic diagnoses were as follows: pancreatic lithiasis, with false-passage formation and ulceration through the duodenal mucosa and exsanguination from a bleeding vessel at the base of the ulcer, and fatty infiltration of the liver.

The intestinal hemorrhage markedly masked the symptomatology, making a clinical diagnosis impossible. Ideally, the radio-opaque calculi are demonstrable on x-ray examination of the abdomen. In this case, the calculi were not observed owing to

*From the Pathological Laboratory, Salem Hospital.

†Formerly, resident in pathology, Salem Hospital.

MEDICAL PROGRESS

THE TREATMENT OF GOUT*

WALTER BAUER, M.D.,† AND FRIEDRICH KLEMPERER, M.D.‡

BOSTON

IN A previous article¹ of this series gout was defined as a hereditary constitutional disease, preeminently of males, occurring at any age and in most cases characterized by recurrent attacks of acute arthritis, caused by deposits of sodium urate crystals. Gout may be manifested only by an asymptomatic hyperuricemia²⁻⁴ that, throughout the life of the patient, may remain the only sign of the disease. Such asymptomatic hyperuricemia, although rarely demonstrated, probably always antedates the first attack of arthritis. Once the hyperuricemia is established it persists throughout life regardless of the incidence or degree of joint involvement. Treatment of gout, in order to be specific, should therefore be based on the knowledge not only of the cause of hyperuricemia but also of the factors that, once hyperuricemia is established, lead to the precipitation of urates in articular and other tissues.

The factors that lead to hyperuricemia in gout have not been fully explained. Theoretically, the elevation in the blood uric acid level may be the result of decreased destruction, increased formation or decreased elimination of uric acid. Since, however, evidence is entirely lacking that uricolysis ever occurs in human beings, the hyperuricemia cannot be ascribed to the first-named mechanism. If it were due to enhanced uric acid formation, a relatively greater excretion would be demonstrable in all patients, as is the case with glucose in diabetes. If, on the other hand, the hyperuricemia were the result of impaired renal function, the uric acid excretion would be decreased, a finding actually observed by many workers. Most gouty subjects when kept on a low-purine diet excrete less than 500 mg. a day, the average being lower than that found in normal persons.^{5, 6} A few cases of increased uric acid excretion are on record,^{5, 7} however, and have led certain workers to postulate that an augmented production of uric acid is responsible for the hyperuricemia of gout.⁷ Although no explanation can be given for these rare cases, it seems reasonable to accept the mass of evidence showing that the daily uric acid excretion of gouty subjects is not increased. It therefore appears that the intermediary purine

metabolism of the gouty patient is normal and that his hyperuricemia is accounted for by a limitation of renal excretion of uric acid that is the end product of purine metabolism.

Hyperuricemia, although an essential feature of gout, cannot be regarded as the sole cause of urate deposition in tissues and arthritis in gout. This is apparent from the following well-established observations. First, hyperuricemia as a result of renal disease or increased formation of uric acid, such as occurs in leukemia and other conditions that lead to an increased breakdown of nuclear tissue, does not cause gouty arthritis except possibly in patients who already have gout as evidenced by the history of preceding attacks or a positive family history. Second, the serum urate concentration does not reflect the severity of the gouty arthritis. It is well known that a patient may have extreme hyperuricemia although clinically the disease is mild; conversely, in some patients with severe disease the serum uric acid concentration hardly exceeds the normal value. In a given patient with gout there is no correlation between clinical symptoms and the fluctuations in urate concentration in the serum. Occasionally patients are seen who have their severest attacks at times when the urate concentration is at its lowest, whereas they may remain asymptomatic at periods when it is high.

The fact that an elevation of urate concentration alone does not necessarily cause precipitation is explained by the strong tendency of sodium urate to remain in supersaturated solution. According to the best available data,⁸ a serum with normal sodium and hydrogen-ion concentrations is supersaturated if the urate concentration exceeds 6.5 mg. per 100 cc. This level must be regarded as an approximation of the true solubility and may have to be revised in the future. Precipitation of sodium urate is a physical impossibility unless the body fluids are supersaturated. Clinical experience that gouty attacks occur only in patients whose serum uric acid concentration is elevated⁸ indicates that the solubility figure given above is approximately correct.

It appears likely, therefore, that the serum of gouty patients is supersaturated in regard to sodium urate. The physicochemical factors that initiate precipitation under these conditions are entirely

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†From the Medical Clinic, Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.
‡The arthritis studies in this clinic were made possible by a grant from the Commonwealth Fund, New York City.
§Associate professor and tutor in medicine, Harvard Medical School, and physician, Massachusetts General Hospital (on leave of absence).
¶Assistant in medicine, Harvard Medical School and Massachusetts General Hospital.

§It should be remembered that even the best methods^{9, 10} for the determination of uric acid are subject to a variety of errors that can be eliminated only by meticulous care and frequent checks. Determinations on whole blood yield lower values than do those on serum. It is possible that the rare exceptions to the above statement are explained by inadequacies of the method.

casional areas of cystic sacculations corresponding to the location of the larger calculi.

The pancreatic parenchyma shows initially an interlobular fibrosis, subsequently developing into an interstitial fibrosis, with consequent replacement of the acini. Only in the later stages does a fibrotic replacement of the islets of Langerhans occur. Therefore, although diabetes mellitus is frequently associated with pancreatic lithiasis, it is not invariably found and, when present, occurs in the latter stages of the disease.

Snell and Comfort¹ in an excellent review of the subject have discussed the physiopathology and symptomatology in a highly enlightening fashion.

As a result of the extensive pancreatic fibrosis and consequent reduction in acini, there is a marked diminution in secretion of the various pancreatic enzymes. The lack of the fatty enzymes, steapsin and lipase, produces the steatorrhea that is so frequently seen. In the case presented above, the fatty nature of the diarrhea was undoubtedly obscured by the intestinal bleeding.

Owing to inadequate elaboration by the pancreas of lipocaic, the hormone functioning in the regulation of the proper deposition of fat in the liver parenchyma, this organ undergoes fatty infiltration and consequent enlargement. The hepatotoxic effect associated with alcoholism is an additional factor.

Abdominal pain is a frequent and a most prominent complaint. This pain is probably due to overdistention of the pancreatic ducts or to temporary spasm of the ampulla of Vater, with obstruction to biliary flow. In addition, there are profound reflex disturbances in the motor and secretory functions of the digestive tract, with consequent production of pain. The pain, however, is distinctly variable in type and location. It is usually intermittent, varying from severe colic to mild, evanescent abdominal distress. It may be confused with biliary colic, but more often it tends to a left-sided extension and may be further projected to the back to the left costovertebral angle and up between the shoulder blades. At times, the pain is excruciating

and associated with nausea and vomiting. Thus, although pain is usually associated with pancreatic lithiasis, it by itself is not of great diagnostic aid owing to its great variability. In this case, the dull, diffuse, nonlocalizing abdominal pain, although in retrospect consistent with pancreatic lithiasis, was by itself in no way diagnostic.

By far the best diagnostic aid is x-ray examination. The finding of radio-opaque shadows along the axis of the pancreas extending to the left of the vertebral column is almost pathognomonic. To be sure, one must differentiate the shadows from those due to gallstones and renal calculi. At times, the calculi are not sufficiently opaque owing to a low calcium content, and in such cases the overlying loops of bowel may obscure the outline of these shadows.

In the absence of positive x-ray findings, the diagnosis of pancreatic lithiasis is a difficult one, because the symptomatology is so variable. The finding of some of the cardinal symptoms—abdominal pain, steatorrhea, hepatomegaly of unexplained etiology and occasionally diabetes mellitus—should, however, make one suspect this disorder and lead to investigation and possible confirmation.

SUMMARY

A case of pancreatic lithiasis with sinus-tract formation and fatal intestinal hemorrhage due to erosion of a blood vessel is presented. The theories of pancreatic calculus formation and symptomatology are discussed. The importance of x-ray examination as a diagnostic aid is emphasized.

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Correction. In the article "Treatment of Meningococcic Meningitis with Penicillin" by Drs. Manson Meads, H. William Harris, Bernardo A. Samper and Maxwell Finland, which appeared in the October 12 issue of the *Journal*, the second and third sentences in the section "Tests for Sensitivity of Strains" on page 512 should be changed to read as follows: "One strain was completely inhibited by 0.36 units per cubic centimeter, 3 by 0.18 units, and 1 by 0.09 units. The first was obtained from Case 7; the organism obtained after eleven days of penicillin therapy in the same case was also tested and showed an increase in resistance, 0.71 units per cubic centimeter being required to inhibit completely its growth."

thing and lessens the chance of accidental jolting. At compresses every three hours are a useful adjunct, although an occasional patient derives greater relief from cold packs. Moist heat is always preferable to dry heat. Diathermy as a rule is not tolerated well.

INTERVAL TREATMENT

Ideally, the treatment of gouty subjects between acute attacks should be aimed at the prevention of the attacks and of complications. In accordance with a widely disseminated belief that adherence to a rigorous purine-free diet reduces or eliminates acute seizures and sufficiently alters the course of the disease to prevent chronic arthritis and the complications of gout, countless gouty patients have been subjected to undue and sometimes serious nutritional restrictions. Although it is well established that such a regimen slightly reduces the serum uric acid level, a careful survey of the past and current literature reveals the astonishing fact that conclusive evidence pertaining to the effect of dietary restriction of purine intake on clinical gout is entirely lacking. Talbott¹² observed no effect on the frequency or severity of the acute attacks in a group of patients maintained on a carefully measured low-purine diet. Likewise, we have seen no therapeutic effect from a low-purine diet or any increase in symptoms when patients who had followed such a rigorous regimen returned to a normal, well-balanced diet.

The conspicuous failure of the low-purine diet to control the recurrence of acute attacks of gout has in no way diminished the search for a dietary means of control of the disease. Extensive trials of a diet almost entirely devoid of fat have been conducted. This mode of treatment was initiated because of the following observations. In 1924, Lennox,¹³ found a significant increase of serum urate concentration in starving subjects whose caloric requirements were met by their own adipose tissue. Harding et al.¹⁴ were able to reproduce these changes by feeding excessive amounts of fat to healthy persons. Subsequently Lockie and Hubbard¹⁵ apparently precipitated attacks in gouty patients by excessive feeding of fat and therefore advocated a diet low in fat as a preventive measure. A strictly fat-free diet forms part of the regimen that has been advocated recently by Bartels.¹⁶ At the present time there is no agreement about the value of this diet. According to our experience gouty attacks cannot be precipitated with any regularity by a high-fat intake, nor is the amount of fat contained in a well-balanced diet sufficient to cause significant retention of uric acid.¹⁷ Furthermore, in our experience the omission of fat from the diet has not proved beneficial.

Unqualified abstinence from alcoholic beverages is almost uniformly advocated, and some clinicians consider the ingestion of alcohol the most impor-

tant of all precipitating factors. We have not, however, been able to provoke attacks experimentally by administration of large quantities of liquor. Despite complete abstinence, a large number of patients continue to suffer from repeated gouty attacks. In a previous article we¹ have quoted specific cases that serve to emphasize that the instrumentality of alcohol in precipitating gouty arthritis is unproved.

In outlining a regimen for gouty patients we are guided by the following considerations. The diet should be balanced and should contain adequate amounts of protein, iron and vitamins. Since circulatory complications are frequent in gout, obesity should by all means be avoided. Drastic curtailment of purine intake is inadvisable because it can be accomplished only by a diet composed of a small variety of vegetables and cereals, eggs and dairy products. Such a diet is not only highly monotonous and unpalatable but, if followed for a prolonged period, is likely to lead to serious deficiency states. Few patients are willing to adhere strictly to such a regimen. Moreover, a reasonably low purine intake can easily be accomplished if only the few foods that are listed in Table 1 are omitted from the diet. This restriction offers no hardship to the patient, but there is no pertinent evidence that the

TABLE 1. Purine Content of Certain Foods.

Food	PURINE CONTENT mg./100 gm.
Sweetbreads	825
Anchovies	360
Sardines	300
Liver	230
Kidneys	200
Brains	195
Meat extracts	150

number and severity of acute seizures is thereby reduced. However, since in most cases of gout the elimination of uric acid is diminished, it appears unreasonable to introduce unnecessary amounts of purines. It is possible that the omission of the few foods mentioned retards the growth of tophi, which occasionally in the late stages of the disease form the chief cause of the patient's disability.

Cinchophen has been extensively employed in the interval treatment of gouty arthritis. Its use is advocated in doses of 0.5 gm. three times daily. As precautionary measures against toxic effects a daily fluid intake of 2000 cc., a high-carbohydrate diet and maintenance of an alkaline urine are usually recommended. There is no doubt that cinchophen does cause a temporary increase in urate excretion and so lowers the blood urate level, but because of its toxicity, and since precisely the same results can be achieved without fear of complications by the use of salicylates, we believe that cinchophen should never be employed in the treatment of gout.

Salicylate is the only safe drug known that causes efficient elimination of urates. In the past acetyl-

unknown. The fact, however, that in supersaturated solutions the formation of precipitate is largely independent of the concentration explains the lack of correlation between the serum uric acid level and the incidence of attacks in gout. Whether attacks are possible if the urate concentration of the body fluids falls below the level of 6.5 mg. cannot be decided so long as the magnitude of the true solubility remains uncertain.

It is therefore evident that serum uric acid determination cannot be used as a measure of the therapeutic efficacy of any regimen and that treatment can be evaluated only on a clinical basis. An important reason for the disagreement about the value of various therapeutic measures lies in the extreme variability of the clinical course of gout. It is well known that patients who have been bedridden for months because of rapidly recurring attacks of great severity often, without any known cause, go into periods of complete freedom from joint pain that in some cases last for years. On the other hand, patients are not infrequently seen who, after having had only rare attacks, spontaneously and without any change in regimen lapse into a state of chronic, crippling disease. The nature of the gouty attack is equally unpredictable. Although typically accompanied by extreme pain and all signs of acute inflammation of the involved joint, it may be evidenced only by pain lasting for a short time without any objective signs. The pain and swelling may subside suddenly during the first day or may last for days or weeks, or the attack may even lead to chronic deformity of a joint. Since it is impossible to account for the variations in the natural course of the disease, it is obvious that evaluation of any treatment, whether directed toward prevention of attacks or toward alleviation of the acute symptoms, is extremely difficult. It is owing to this difficulty that in the past many different and contradictory methods of treatment have been proposed.

TREATMENT OF ACUTE ATTACK

The treatment of the acute attacks of gouty arthritis is satisfactory. Colchicum, obtained from the seeds of *Colchicum autumnale* (fall crocus), was first recommended by Alexander of Tralles (525-605) and, as colchicine, remains the drug of choice. Its mode of action in gout is unknown beyond the fact that it does not affect the hyperuricemia or the renal excretion of uric acid. We have seldom seen it fail to bring relief when given properly during the first few hours of an acute attack. When administration is delayed, the effect is less certain, but an attempt to shorten an attack by administration of colchicine is advisable at any stage of the disease. It has fallen into disrepute in times past, undoubtedly owing to the use of impure or impotent preparations in the form of wine or tincture. Therapeutic failures can often be avoided if the drug is always administered as crystalline colchicine. The

preliminary use of a saline cathartic is recommended by some.¹¹

We prescribe 0.5 mg. every hour or 1 mg. every two hours, until relief from pain is obtained or until diarrhea or nausea and vomiting result, when the drug is discontinued. Provided the patient is kept at bed rest, pain and swelling usually subside within twenty-four to seventy-two hours after the first loose bowel movement. Rarely do the articular symptoms disappear sooner. The ensuing diarrhea is frequently severe enough to require treatment with paregoric; 4 cc. is given following each loose stool until the diarrhea is checked. Bismuth subcarbonate may be used instead of or in conjunction with the paregoric. Once the amount of colchicine necessary to produce such symptoms has been established in a patient, the total dose may be reduced by one or two tablets (0.5 or 1.0 mg.) to avoid severe gastrointestinal symptoms without curtailing the desired effect. The total amount required to alleviate the acute attack varies from 4 to 8 mg. of colchicine and rarely exceeds this quantity.

We have never observed any other untoward effects from crystalline colchicine. Hypersensitivity to the drug is unknown, nor does it lose its efficacy with repeated administrations. The patient should always carry colchicine. The appearance of any prodromal symptoms or the first twinges of articular pain call for immediate institution of therapy. If these rules are followed, the patient will be spared many prolonged and incapacitating seizures. Some workers unwisely object to the side action of colchicine and delay therapy until the attack has fully developed.

We can find no indications for the use of cinchophen and substances closely related to it, either alone or in conjunction with colchicine. To be sure, the risk attendant on their administration—primarily that of acute liver necrosis—is statistically small, but minor symptoms of toxicity are a more frequent annoyance to the patient and serve as warning signals for immediate cessation of therapy. In omitting these drugs, we are guided by the fact that colchicine, when given properly, is not only entirely safe but also much more effective. Morphine or codeine may be needed to ensure comfort before the colchicine effect is secured. At the time of the seizure, no dietary measures other than those given for any painful illness of short duration are required. Patients rarely desire anything more than liquids and soft foods, and a daily fluid intake of 3000 to 4000 cc. should be encouraged.

Absolute bed rest is always indicated for the duration of the attack, whether or not weight-bearing joints are involved. Premature resumption of normal activity not infrequently precipitates an exacerbation. Avoidance of even normal joint use prevents minor trauma, thereby shortening the period of incapacitation. Protection of the affected part by a cradle eliminates the pressure from bed-

thing and lessens the chance of accidental jolting. Hot compresses every three hours are a useful adjunct, although an occasional patient derives greater relief from cold packs. Moist heat is always preferable to dry heat. Diathermy as a rule is not tolerated well.

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Salicylate is the only safe drug known that causes efficient elimination of urates. In the past acetyl-

salicylic acid (aspirin) has been recommended in doses of 5 to 6 gm. on three consecutive days of each week.¹⁸ Figure 1 demonstrates the changes in the serum level and excretion of uric acid that take place on this regimen. During the seven days

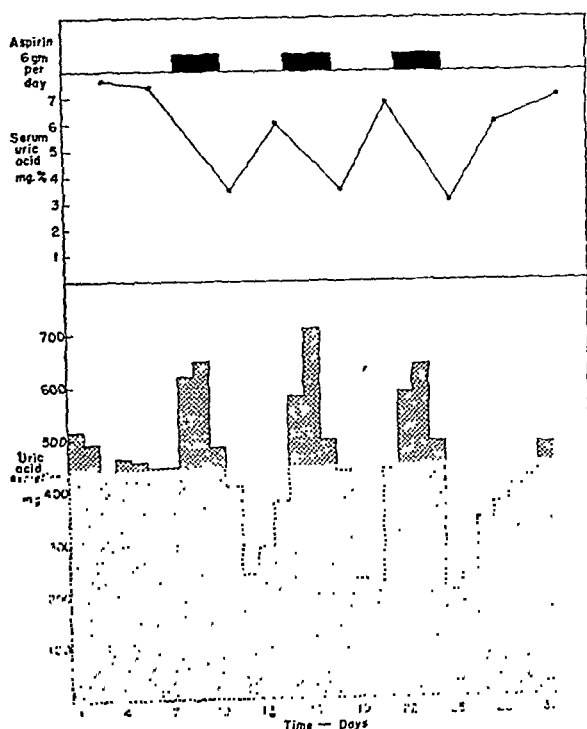


FIGURE 1. The Effect of Intermittent Acetylsalicylic Acid Medication on the Serum Uric Acid Level and the Uric Acid Excretion.

preceding administration of salicylates the average daily uric acid excretion amounted to 466 mg. During the twenty-four-day period of intermittent administration of salicylates the average was 433 mg. It is apparent that, although marked urate diuresis was caused by the administration of acetylsalicylic acid, a corresponding amount of urate was retained during the immediately ensuing period, with the result that the total amount of urate excreted was not significantly altered by this regimen. The serum urate level likewise underwent fluctuations and reached high levels on the days when no salicylate was given. After a few months of such treatment tolerance is developed and the serum uric acid becomes stabilized at its usual level.

Salicylates are effective in promoting the excretion of uric acid only when given in large amounts. They are ineffective in doses of less than 4 gm. a day, and we¹⁹ have seen actual retention of uric acid with marked increase in the serum concentration when doses of 1 to 2 gm. were given. Striking reduction of the serum urate concentration is observed when salicylates are given in continuous daily doses of 5 to 6 gm. Under these conditions a lowering of the blood urate level to one third its

original level is frequently observed. Figure 2 illustrates the typical changes that occurred in a patient treated with continuous daily doses of 5 gm. of acetylsalicylic acid. It is evident, however, that the reduction of the serum urate concentration is temporary, and a gradual return to the original level usually occurs within about three months.

Clinical observation has proved that it is impossible to prevent attacks of gouty arthritis by continuous administration of salicylates. This is not surprising in view of the fact that it is impossible to maintain the serum uric acid permanently below the critical level of about 6.5 mg. Therefore, we advise neither continuous nor intermittent administration as a routine procedure. On the other hand, in a number of patients studied while in a state of rapidly recurring attacks we have not observed the recurrence of new joint symptoms during the first few weeks of treatment with massive doses of acetylsalicylic acid. Only more extensive studies will enable us to decide whether in these patients the cessation of attacks was caused by the administration of salicylates or whether we were dealing with the natural remissions that occur so frequently in the course of gouty arthritis. These studies, although inconclusive as to the therapeutic value of salicylates, demonstrate clearly that, without any inherent risk, results can be obtained by their use that equal those ascribed to cinchophen. Gastrointestinal symptoms, occasionally encountered after

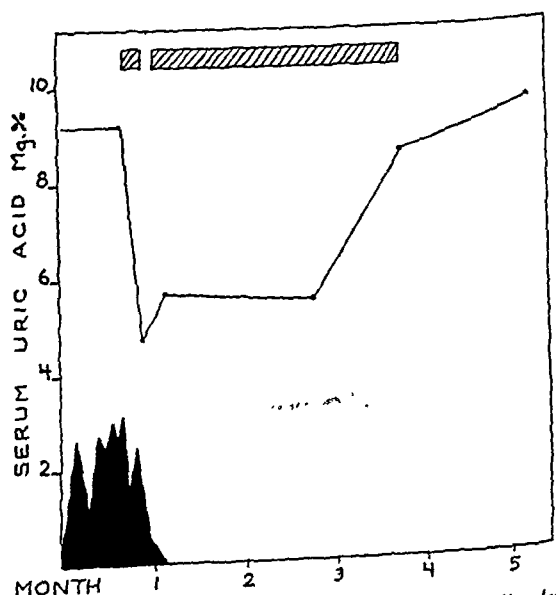


FIGURE 2. The Effect of Continuous Acetylsalicylic Acid Medication on the Serum Uric Acid Concentration. The shaded area represents the administration of 5 gm. acetylsalicylic acid daily. The black area signifies the incidence of attacks of gouty arthritis.

large doses of acetylsalicylic acid, can easily be controlled by the administration of equal amounts of sodium bicarbonate. There is no justification for

giving large doses of salicylates continuously except in patients who have lapsed into a state of rapidly recurring attacks of gouty arthritis.

Some authors^{20, 21} advise the giving of 10 gm. of glycine daily for three days of each week in conjunction with salicylates as another means of augmenting the output of urates. We have never employed this combination, but our experience with glycine alone has been disappointing. We have seen no beneficial effects from the administration of thiamine chloride. The administration of small daily doses of colchicine (1 mg.) in the interval, as suggested by some,¹² although harmless, has had no preventive value.

The injection of purified uricase, prepared from pig's liver, has recently been attempted by Oppenheimer and Kunkel.²² These authors were unable to demonstrate any action of the injected enzyme on the uric acid concentration in the blood of men.

Chronic gouty arthritis is least amenable to treatment of any form of the disease. In this stage, acute attacks are relatively infrequent and mild. The patient's disability and pain are due primarily to the permanent joint changes that have been caused by the preceding acute attacks. Some of our patients feel certain that the giving of 0.5 mg. of colchicine three times a day provides a measure of relief. Regular rations of salicylates are often necessary for the control of pain. Active or passive exercise should be prescribed whenever possible to prevent increasing limitation of the involved joints, but severe pain may make immobilization of a joint imperative. In selected cases, operative correction of joint deformities has yielded fair results. Application of foot pads or special shoes may be indicated. Troublesome tophi can usually be excised without precipitating an attack of gout.²³ We know of no special benefit derived from spa therapy.

The cardiovascular disease and vascular nephritis that so frequently complicate gout are not preventable and must be treated according to the specific needs of the patient. The unexplained high incidence of urinary calculi in gouty subjects, amounting to 12 per cent in Hench's²⁴ series, can probably be reduced if a liberal daily fluid intake (3000 cc.) is encouraged in all patients. Alkalinization of the urine by the daily administration of 8 to 16 gm. of sodium citrate is advised in those patients who are known to have formed uric acid stones. It is not recommended as a routine procedure because calcium phosphate stones are known to have occurred in association with gout.¹⁷

SUMMARY

Gout, which is a hereditary disorder, cannot be prevented or cured. Interval treatment with diet, drugs or a combination of both as advocated to date has been disappointing. After a careful survey of personal results and a review of the literature, it is concluded that there is no pertinent evidence that these measures alter the clinical course of the disease or even lessen the incidence of attacks. The treatment of the acute attack is highly satisfactory, colchicine being the drug of choice.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30461

PRESENTATION OF CASE

First admission. A sixty-seven-year-old cook entered the hospital because of abdominal swelling.

The patient was essentially well until one year before entry, when he developed orthopnea, exertional and nocturnal dyspnea, which had increased in severity, especially during the month before entry. Three or four weeks before entry he developed a cough productive of a small amount of white sputum. Six days prior to admission, swelling of the abdomen and ankles appeared and progressed to the point where he was unable to work.

The past history was essentially negative except for the imbibition of two or three glassfuls of beer and occasional drinks of whisky daily for twenty years and, before that, two or three pints of beer and about a gallon of wine daily for some years.

Physical examination showed an obese, slightly cyanotic, orthopneic and dyspneic man. The anteroposterior diameter of the chest was increased, and its expansion limited. Breath sounds were diminished toward both bases, more so on the right, with a few crackling and moist rales. Loud wheezes and rhonchi were heard throughout the chest on inspiration and to a less degree on expiration, persisting after cough. The heart was moderately enlarged, with the apex 4 cm. beyond the mid-clavicular line. The rate was regular. There was no pulse deficit. A loud, grating "meat slicer" murmur was heard over the precordium, loudest over the aortic area, and was transmitted to the neck vessels. No diastolic murmurs were audible. The aortic second sound was greater than the pulmonic. The abdomen was distended, with a fluid wave and shifting dullness. The edge of the liver extended 10 cm. below the costal margin and was slightly tender. There was moderate scrotal edema. The prostate was diffusely enlarged and firm. There was slight pitting edema of the legs.

The blood pressure was 135 systolic, 75 diastolic. The temperature was 100°F., the pulse 80, and the respirations 25.

*On leave of absence.

Examination of the blood showed a red-cell count of 5,540,000, with 95 per cent hemoglobin, and a white-cell count of 7250, with 61 per cent neutrophils. The urine gave a + test for albumin and, after the first day, a green or olive reaction with Benedict's reagent. A blood Hinton test was negative. An electrocardiogram revealed auricular flutter, with four-to-one block, the ventricular rate being 75, and the auricular 300. The axis was normal, T₁ inverted, T₂ and T₃ upright, and T₄ low but upright. An x-ray film showed marked enlargement of the heart in the region of the left ventricle. The right border was also prominent. The transverse diameter was 17.2 cm., and the internal diameter 32.2 cm. In the left oblique view an area of calcification was seen in the region of the aortic valve. The hilar shadows were prominent, but the vascular markings were only slightly increased. There was no fluid in the pleural cavities. A plain film of the abdomen showed moderate enlargement of the liver. The lower border extended about 8 cm. below the costal margin laterally.

The patient was given 0.3 gm. (4½ gr.) of digitalis daily for six days, — thereafter, 0.1 gm. daily, — 1 gm. of ammonium chloride three times a day and occasional intravenous injections of Mercupurin. The fluid intake was limited to 1500 cc. He failed to show any spectacular diuresis at first, but the edema gradually decreased. The orthopnea and dyspnea became much less. On the eleventh hospital day, the fasting blood sugar was 210 mg. per 100 cc., the nonprotein nitrogen 32.5 mg., and the protein 7.7 gm., with an albumin-globulin ratio of 1.4. A cephalin-flocculation test was +++ in twenty-four hours and ++++ in forty-eight hours. A bromsulfalein test gave 70 per cent retention.

A urine examination on the day of discovery of high blood-sugar level revealed an orange reaction for sugar and a ++ test for acetone. He was given a high carbohydrate diet, and the diabetes was controlled with insulin. An electrocardiogram on the twelfth hospital day revealed conversion of the auricular tachycardia to fibrillation. The patient improved for a few days, but with increased fluid intake the output decreased and there was recurrence of the edema, which was then treated by limitation of the fluid intake and diuretics. On the thirtieth hospital day, however, he had ascites and moderate pitting edema of the ankles. The liver edge was felt 8 cm. below the costal margin. The heart rate was slow (40) but regular.

He improved some in the next six days and was discharged home on 0.1 gm. of digitalis daily, 1 gm. of ammonium chloride three times a day, a high-vitamin diet and provision for the control of the diabetes.

Final admission (two months later). After discharge the patient was followed in the Out Patient Department, where he was given occasional intra-

ous injections of Mercupurin. On one occasion, 3500 cc. of deep-straw-colored ascitic fluid, with a specific gravity of 1.018, was withdrawn, with marked relief. During the first month the heart rate was 60, with frequent bigeminy. Although the patient claimed that he followed the regimen prescribed for him, the fluid reaccumulated and he became increasingly dyspneic and orthopneic and extremely weak and tired. He was admitted to the hospital.

Physical examination showed marked edema of the legs, moderate respiratory distress, but no cyanosis. The neck veins were distended. The mucous membranes and tip of the tongue were smooth. Breath sounds were depressed over both bases, more so on the right, with absent tactile fremitus and evidence of fullness. The heart was regular but slow. All the sounds were distant and of poor quality. There was a Grade III systolic murmur, which masked the first sound over the entire precordium. The abdomen was markedly distended. The liver edge was ballotable six fingerbreadths below the costal margin. The spleen was enlarged but not palpable. The lower extremities showed moderate pitting edema, which gradually diminished to slight swelling of the umbilical region.

The blood pressure was 140 systolic, 70 diastolic. The temperature was 99.4°F., the pulse 40, and the respirations 22.

Examination of the blood showed a red-cell count of 3,900,000, with 12.5 gm. of hemoglobin, and a white-cell count of 10,050, with 69 per cent neutrophils. The urine gave a ++ test for albumin and was negative for sugar. The stools were guaiac negative. The venous pressure was 16 mm. An electrocardiogram showed auricular fibrillation, with a rate of 55. The axis was normal. There were a few premature ventricular beats. T₁ was flat or slightly inverted, ST₂ depressed, T₂ low, and T₃ and T₄ flat. The fasting blood sugar was 102 mg. per 100 cc., the nonprotein nitrogen 22.5 mg., and the protein 7.5 gm. An x-ray film of the chest showed a large amount of fluid in the right pleural cavity, extending to the level of the eighth rib in the midaxillary line. Some increase in the vascular markings was apparent throughout both lungs. The left costophrenic angle was hazy.

The patient was kept on essentially the same program of therapy as previously. On the third day he had a profuse epistaxis, which stopped spontaneously. On the fifth day, 3000 cc. of straw-colored fluid was withdrawn from the abdomen. There was temporary improvement, but his condition became progressively worse and he died on the eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS: In summary, this is the case of a sixty-seven-year-old man who came in with a history of progressive dyspnea and edema

and died two months later in a state of considerable fluid retention, in spite of fairly intensive therapy directed against it. It seems obvious that there are three main features. One is heart disease; another is the question of liver disease; and the third is diabetes, which we know that he had. Can all these findings be explained on a diagnosis of heart disease alone, and if so, what was the etiology? I believe that I can answer the first question but not the second.

It seems to me that, from the evidence at hand, all the findings described here cannot be explained by a diagnosis of heart disease alone. One of the greatest discrepancies is the finding of a venous pressure of 16 mm. (just above normal), with ascites and edema of the feet and ankles and so forth. Another feature that is a little unusual for heart disease alone is the appearance of ascites, presumably before the ankle edema. At any rate, when the patient first came in, ankle edema was slight and ascites quite well marked. That may be seen in cases in which the venous pressure is high, as in constrictive pericarditis or tricuspid disease, but in the ordinary course of congestive heart failure, especially that progressing from the left to the right side of the heart, such a sequence of events is unusual. The liver size too seems out of proportion to the venous pressure if one can credit the one measurement. Although this was taken at a time when the signs of fluid retention were quite marked, very likely we have another complication to consider. At this point I should like to ask the radiologist whether or not he thinks that the heart shadow was particularly enlarged.

DR. LAURENCE L. ROBBINS: Without much question in this film, which apparently was taken at the time of the first admission, the heart shows definite left ventricular enlargement. The area of calcification that is described in the note I presume is this area here, which is perfectly consistent with calcification in the aortic valve. One cannot say from the films alone that it was definitely within the heart, but it probably remained within the heart during fluoroscopy. These films, taken some three months later, are consistent with congestive failure.

DR. WILLIAMS: Do you think that the heart shadow is large?

DR. ROBBINS: There is slight to moderate enlargement.

DR. WILLIAMS: That may be an important point in making a decision about the underlying disease. It seems to me that the heart shadow should have been larger if this much fluid retention resulted from heart disease alone. Of course in a young person one should always think of mitral stenosis, with or without tricuspid disease, to account for an apparently predominant right-sided heart failure. In an elderly patient, such a diagnosis is possible but much less likely, and in this case I shall have

to throw it out. The necessary murmurs are not present, and the x-ray findings do not suggest mitral disease. High-grade tricuspid disease is hardly ever seen in the absence of mitral disease, except in rare congenital cases. It seems fairly obvious that there was some involvement of the heart. We have cardiac enlargement and a definite systolic murmur to back up that supposition, and the electrocardiographic changes are also indicative of heart disease, especially in the presence of significant arrhythmia, both flutter and fibrillation.

What is the etiology of the cardiac lesion? The murmur suggests aortic stenosis. Calcereous aortic stenosis usually occurs at this patient's age. Apparently the aortic second sound was heard, as it may be even in the presence of a fairly high degree of aortic stenosis. If an attempt is made to explain this whole picture on that basis, I should be happier about not hearing an aortic second sound, because the degree of aortic stenosis would need to be great, unless there was a complicating disease of the myocardium in addition. Coronary heart disease is a good possibility, yet one would not expect to find extensive myocardial involvement in the absence of previous infarction. Certainly from the history and the electrocardiogram there is no evidence that such an episode had ever taken place. So I cannot say much about the etiology of the heart disease, beyond saying that I think the patient probably had aortic stenosis.

How about liver disease? First of all, he had a good and a prolonged alcoholic history, and the laboratory tests are in keeping with the diagnosis of cirrhosis. The high grade of bromsulfalein retention and the positive cephalin-flocculation test, in the absence of any evidence of biliary obstruction, are certainly in favor of a diagnosis of cirrhosis. The liver size is also in keeping, and I think that I can explain the ascites better by assuming that the patient had a complicating liver disease. One often hears the clinical statement to the effect that when ascites develops in cirrhosis the liver must be small, but that is not always so.

How about other possible causes of the edema? We know that the serum protein, at least the total protein, was normal throughout. The albumin-globulin ratio was never more than slightly abnormal. Could the patient have had an obstruction of the inferior vena cava? There is no evidence of such an episode, and it would not explain the liver enlargement.

There is one other disease that must be considered, namely, hemochromatosis. This man presumably had liver disease, probably cirrhosis, in the presence of mild diabetes and cardiac involvement, with enlargement of the heart and at least some cardiac failure. To my knowledge hemochromatosis is almost never seen without pigmentation of the skin, but in one of these conferences anything can happen. I should like to ask Dr.

Castleman if any statement was made about skin pigmentation.

DR. BENJAMIN CASTLEMAN: No.

DR. WILLIAMS: In this stage of the disease one would almost certainly expect to see pigmentation of the skin. I just mention hemochromatosis as a possibility. It may produce destructive myocardial lesions as a reaction to the presence of pigment deposited in the heart muscle.

My final diagnoses are aortic stenosis, probably calcareous, cardiac enlargement, congestive heart failure, alcoholic cirrhosis of the liver, diabetes mellitus and, possibly, hemochromatosis.

DR. JOSEPH C. AUB: The quantity of ammonium chloride given was small (3 gm.) for the amount of edema. Maybe it was not effective so far as diuresis was concerned. Also, I do not believe that fluid in the chest rules out the possibility of cirrhosis. A good many of our cirrhotic patients have fluid in the right side of the chest. I do not know why.

DR. WILLIAMS: I meant to mention the fact that the presence of fluid in the chest is not against heart failure or cirrhosis.

A PHYSICIAN: Would there be any retention in fluid?

DR. WILLIAMS: Yes, more or less retention.

DR. PAUL D. WHITE: As I remember the story there seemed to have been hardly enough dyspnea to explain chronic left-sided, followed by chronic right-sided, heart failure. Is that true?

DR. WILLIAMS: He had dyspnea for a year. It is not described in great detail. I do not know whether it was present all the time.

DR. WHITE: To have cardiac cirrhosis one must have a lesion resulting in marked right-sided heart failure, which usually follows an extremely chronic degree of left-sided heart failure. Since that was not striking in this case, cardiac cirrhosis would seem less likely than alcoholic cirrhosis.

DR. WILLIAMS: I think constrictive pericarditis can be ruled out by the electrocardiogram as well as by the venous pressure.

CLINICAL DIAGNOSES

Calcereous aortic stenosis.
Cardiac hypertrophy.
Portal cirrhosis of liver.
Diabetes mellitus.

DR. WILLIAMS'S DIAGNOSES

Aortic stenosis (calcareous).
Cardiac enlargement.
Congestive failure.
Cirrhosis of the liver (alcoholic).
Diabetes mellitus.
Hemochromatosis?

ANATOMICAL DIAGNOSES

Rheumatic heart disease.
Endocarditis, chronic, rheumatic, of mitral and aortic valves.

- Calcareous aortic stenosis.
- Cardiac hypertrophy and dilatation.
- Pulmonary congestion and edema.
- Hydrothorax, right.
- Ascites.
- Peripheral edema, moderate.
- Chronic passive congestion.
- Cirrhosis of liver, cardiac, slight.
- Chronic thyroiditis (Riedel's struma).

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this man showed an enlarged heart, weighing 550 gm.

There was no disease of the tricuspid or pulmonary valves.

We found 500 cc. of straw-colored fluid in the abdomen and 1000 cc. in the right chest. The lungs showed congestion and some edema. The liver was enlarged, weighing a little under 2000 gm., and in gross showed little if any evidence of cirrhosis, perhaps a fine granularity but certainly not a portal cirrhosis. There was distention of the central veins grossly, and microscopically there was dilatation of all the sinusoids, with narrowing of the liver cords and a little cellular infiltration in places (Fig. 2), a picture characteristic of a fairly severe



FIGURE 1. Photograph of the Heart.

Note the calcareous stenosis, as well as the shortening and thickening of the chordae tendineae of the aortic leaflet of the mitral valve.

There was rheumatic involvement of the mitral valve but not enough to produce a severe stenosis. The chordae tendineae were shortened and thickened, and the leaflets themselves were fibrotic. The aortic valve also showed rheumatic involvement (Fig. 1). There was interadherence of the cusps of the aortic valve for a distance of almost 1 cm. from their commissures. In addition there were calcareous masses on the aortic side of the valve in and above the sinuses of Valsalva and also on the endocardial side of the valve. So we have an aortic calcareous stenosis, definitely rheumatic this time, to account for the enlarged left ventricle.

degree of chronic passive congestion. There were scattered foci of early fibrosis, and I believe that there is sufficient evidence for a diagnosis of early cardiac cirrhosis. It is quite unusual to have this much cirrhosis with the first attack of heart failure. Cardiac cirrhosis usually occurs only after two or three attacks, whereas this patient, at least from the history, had had just one.

DR. WHITE: He may have had more prolonged disease than we know about.

DR. CASTLEMAN: Another interesting finding in view of the diabetes was a severe chronic thyroiditis

of the Riedel struma type. There must have been little activity of the thyroid gland. With severe thyroid impairment one would ordinarily expect a low blood sugar rather than diabetes. Is that not so, Dr. Aub?

DR. AUB: The fasting blood sugar ought to be normal. The sugar curve might be abnormal in hypothyroid disease. Hyperthyroidism has a blood-sugar curve reminiscent of diabetes, but it starts off with a normal blood-sugar level.*

DR. HOWARD B. SPRAGUE: Do you believe that the alcoholic history had anything to do with

In reading this history I could not differentiate, but with the liver findings and with aortic stenosis of rheumatic origin I thought that he must have had cardiac cirrhosis, because on referring to Dr. White's* book I find the statement, "Cirrhosis of the liver due to heart disease, although infrequent, is most commonly noted in those who have had chronic or recurrent congestive failure secondary to rheumatic heart disease."

DR. WHITE: I think this is a case in point in which we cannot distinguish clinically. Although Dr. Castleman found no alcoholic cirrhosis, alco-

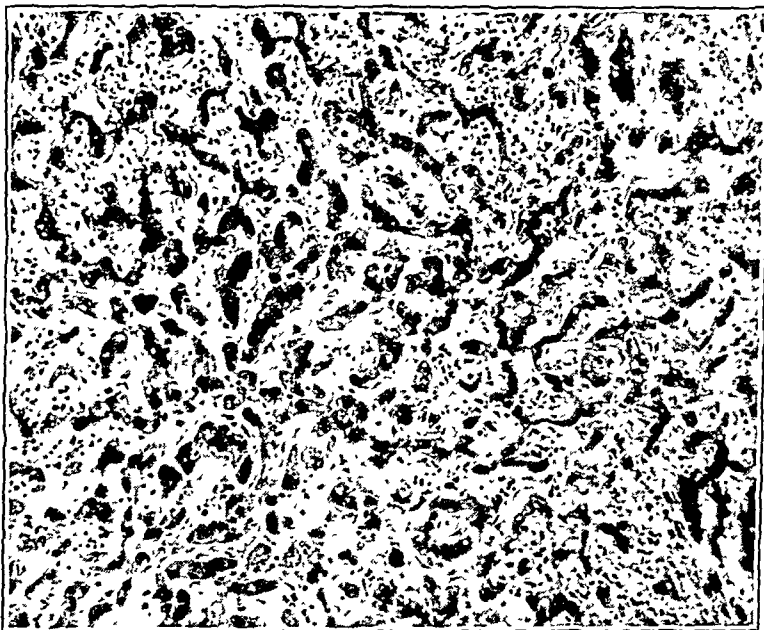


FIGURE 2. Photomicrograph of the Liver.

making the liver hypersensitive to chronic passive congestion?

DR. CASTLEMAN: I do not believe so, because if there was any evidence of alcoholism in the liver we should have seen a fatty change with perhaps hyaline granules in some of the liver cells or a little portal cirrhosis. We found nothing to suggest it.

DR. WHITE: If a patient has had enough congestion, I suppose that he might have impairment of function that would resemble primary liver disease.

DR. WILLIAMS: One point that might have settled the thing from the beginning would have been an accurate observation on the state of the neck veins. A good clinical observation of neck veins is almost as good as direct measurement of the venous pressure. Often there is an early increase in venous pressure. A statement is made in the history, but the observation was made later. I wonder whether the degree of congestion was out of proportion to the size of the heart. There seems to have been a terrific amount of congestion for a moderately enlarged heart.

A PHYSICIAN: How would you distinguish between cardiac cirrhosis and portal cirrhosis at the bedside?

holism may possibly have been something of a factor in preparing the field for the cirrhotic change when his heart finally failed.

DR. SPRAGUE: Of the hundreds of cardiac cases that we see here, we encounter this picture only rarely.

A PHYSICIAN: What about the spleen?

DR. CASTLEMAN: It was not enlarged, weighing about 200 gm. It certainly could not have been felt and probably could not have been shown by x-ray to be enlarged.

A PHYSICIAN: Would the finding of esophageal varices have helped?

DR. CASTLEMAN: Yes; that would be a differentiating point between portal and alcoholic cirrhosis. They apparently were not observed.

DR. REED HARWOOD: Was there coronary sclerosis or evidence of disease in the myocardium?

DR. CASTLEMAN: There was slight narrowing of the coronary arteries, but no evidence of scarring of the myocardium.

*White, P. D. *Heart Disease*. Third edition. 1025 pp. New York: Macmillan Company, 1944. P. 557.

CASE 30462

PRESENTATION OF CASE

A seventy-one-year-old housewife was admitted the hospital for study.

For many years the patient had had intermittent abdominal pain. Fifteen years before entry, following an attack of cholecystitis, a cholecystectomy and probably a choledochostomy were done, with considerable immediate relief. She continued, however, to have intermittent attacks of vomiting and epigastric pain associated occasionally with dark urine and once with jaundice for a day. Four months prior to admission she began to have bouts of crampy epigastric pain on getting up in the morning, so that she was forced to go back to bed several hours. These occurred about once a week. In the next two months the pain increased in severity but never radiated to the back or to the shoulder. There was occasional vomiting of bile-stained material. She gradually became disabled. Three weeks before admission she entered hospital in another city. A gastrointestinal series taken there was said to have shown a diaphragmatic hernia. Plain films of the abdomen showed gas in the large intestine. There was some improvement in the abdominal pain, but she was referred here for further study. She had been constipated for years, and there had recently been no change in the stools.

Physical examination showed a well-nourished, slightly pale woman in no discomfort. The heart was not enlarged. Apical and aortic (Grade I) systolic murmurs were heard. The lungs were clear, except for occasional squeaks. The abdomen was distended. Peristalsis was active and of normal rhythm. In the epigastrium there was tenderness to deep pressure, but no masses were palpable. The lower extremities were edematous up to the lower thigh.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 75, and the respirations 20.

The white-cell count was 9100, with 12 gm. of hemoglobin. The nonprotein nitrogen was normal, and the serum protein 5.8 gm. The specific gravity of the urine was 1.010; it showed a + test for albumin, and the sediment contained 30 white cells and 3 red cells per high-power field. A blood Hinton test was negative. A van den Bergh test was too low to read. Plain films of the abdomen showed a considerable amount of gas in the colon and a moderate amount in the epigastric region, probably in the stomach; no definitely dilated loops of small bowel were visible.

The patient was given daily intravenous fluids. A Miller-Abbott tube was passed with some difficulty to the ligament of Treitz. The following day about 15 cc. of barium was injected through the tube, which by that time was in the lower ileum.

and filled a nondilated loop. Peristalsis was not active, however, and the barium did not pass along the bowel during the short period of fluoroscopy. A film taken one hour later showed the barium in the cecum. No dilated loops of small intestine were visible. A twenty-four-hour film showed all the barium in the right side of the colon. No evidence of intestinal obstruction was seen.

The patient continued to have abdominal discomfort and vomited everything she ate. On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: We are asked to discuss a case of crampy epigastric pain, vomiting and abdominal distention in an elderly woman with an old history of gall-bladder disease whose physical examination was essentially normal except for edematous legs. If there is a clue about what part of her anatomy was at fault, I fail to find it, and the laboratory work offers no help. Perhaps the attempt to fill the small intestine with barium indicates that the clinicians' chief interest was in the small bowel. One must assume that they knew more about her than we do, for I am certain that I should not operate on anyone with the facts at hand. Assuming, then, that something was at fault with the small intestine, — the location of pain and persistent vomiting tend to bear that out, — what should we consider?

The story suggests that she did not have obstruction, but rather impediment to the passage of intestinal contents. A band or adhesion is statistically the likeliest cause of this.

We know that the patient had had an operation on the gall bladder. Adhesions of the duodenum to the gall-bladder bed with angulation are not at all infrequent, but the clinicians appear not to have been interested in that region, since they injected barium into the lower ileum. Certainly an adhesion of the small intestine below the duodenum to the gall-bladder bed is unusual. What else could have been at fault? Tumors of the small bowel occur and may have obstruction as their first symptom. Practically any type of tumor could be considered and not ruled out. Furthermore, interference to the circulation of the bowel at this patient's age is not rare.

Mesenteric venous thrombosis is a possibility, and it could perhaps best explain the apparent atony of the small bowel observed under the fluoroscope. A four-month history, however, is unusual for this condition. We are told that the pain at no time radiated to the back, which is unlikely when the mesentery is involved. A complication of a Meckel's diverticulum might be considered. It seems pointless to continue with a catalogue of all the minor possibilities that can and probably should be thought of in connection with this patient.

Since a diagnosis is asked for, I shall say that this patient had venous thrombosis of a segment of mesentery of the small bowel, probably in the lower jejunum or upper ileum, which was not sufficient to cause necrosis of the bowel but which did prevent normal peristalsis and so produced the symptoms.

CLINICAL DIAGNOSIS

Postoperative adhesions.

DR. HAMLIN'S DIAGNOSIS

Mesenteric venous thrombosis.

ANATOMICAL DIAGNOSIS

Carcinoma of pancreas, with peritoneal metastases.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: As Dr. Hamlin has indicated, the available clinical data on this patient were extremely meager, but the case does bring up the question of a differential diagnosis of atony of the small bowel with abnormal peristalsis. Dr. Hamlin chose venous thrombosis; the surgeon in charge of the patient inclined toward adhesions caused by the previous gall-bladder operation. Another cause of disturbed peristalsis is carcinomatous infiltration of the visceral peritoneum of the small bowel, and that is what this patient had. There were numerous small tumor nodules over the small bowel, one of which was biopsied and proved to be adenocarcinoma. The primary tumor was a baseball-sized mass in the head of the pancreas. A liter of ascitic fluid was aspirated before the abdomen was closed.

We have since heard that the patient died five months later.

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THE FREEDOM

A YOUNG infantryman, writing from the Italian front last winter, gave his views on the problem of promised freedoms. The four freedoms, according to this concept, can be included in the one freedom — freedom of thought in its broadest sense. He wrote: "The other three are subsidiaries. . . . Freedom of religion is but a phase of direct thought. Hatred and fear are curses which can be lifted only by 'right thinking.' . . . Freedom of thought should be interpreted in a very positive light — the necessity for true thought, and it should imply the forward step from freedom-to-think-as-you-please to the compulsion to seek out the truth." This foxhole philosophy arose out of a soldiers' discussion of war ideals and issues; it does its bit

toward making us believe that the soldier, too, realizes his stake in the war and the peace, and sees no advantage in risking his own life in combat unless some considerable portion of the human race is going to benefit by his sacrifice. Under the circumstances there is something either stupid or sinister in the recent legislative attempt to deny political information to the soldier after giving him the vote; to deny him, in other words, that very freedom of thought for which he had been given to understand that he is fighting.

Freedom of thought and its more concrete ramifications, such as freedom of speech, freedom of the press and freedom to worship, are actually highly elusive qualities that must be wooed and fought for and cherished, over and over again. No ruler, however altruistic, however freedom-loving in principle, can hold power long without putting restrictions for others on the very freedom that he professes to love so well. A subversive tendency is being shown in our own government, where, it is said, various department workers are forbidden to question department policies, unless they care to run the risk of losing their jobs. Freedom of thought cannot be tolerated, apparently, on a one-track road, and no desire for the truth, however burning, can be permitted to interfere with departmental expediency.

Everywhere, on a desperately contested battle front, we are fighting to protect our basic freedom against assaults from without. We must not forget, however, that the "compulsion to seek out the truth" must be constantly protected from those who would seek to destroy it from within — even from some who, with apparent sincerity, give it their daily blessing.

GLOBAL EPIDEMIOLOGY

PERHAPS nothing is a better illustration of the intricacies and all-inclusiveness of modern medicine than one of many problems that faced the Preventive Medicine Service of the Office of The Surgeon General prior to and after the entry of the United States in World War II. This particular problem concerned the assembling, evaluation and dissemination of data regarding medical, health and sanitary conditions for all localities in which military

forces might be stationed. Because of the global character of the conflict it soon became apparent that information should be available for every corner of the world, varying from Arctic regions to the tropics, from arid deserts to humid jungles and from areas with adequate public-health control to those in which such facilities were lacking, indeed in which the dangers of disease were much greater than those of combat.

The Medical Intelligence Division of the Preventive Medicine Service was established in June, 1941, to handle the problem, and this division, to which two officers were originally assigned, has now grown to comprise eleven officers, five civilians of professional grade and a clerical staff of fifteen. Surveys covering one hundred and ninety areas have been prepared. The data included are as follows: geography and climate; public health, including health services, water supplies, sewage disposal, insects and animals, poisonous plants and foods, food and dairy products, and miscellaneous problems of sanitation; medical facilities, including hospitals, medical personnel and medical institutions; diseases, arranged according to mode of spread; a summary; and a bibliography. The enormity of the task of assembling these facts is apparent, particularly since many of them could be obtained only from obscure sources or by personal interviews. Equally clear is their value not only to the military forces but also to those interested in the broad aspects of preventive medicine, and the publication of these surveys, necessarily with the deletion of matters of military significance, should be enthusiastically welcomed.

The first volume of *Global Epidemiology** consists of two parts: the first includes India and the Far East, and the second, the Pacific area. The listed authors, Brigadier General J. S. Stevens, chief of the Preventive Medicine Service, Office of The Surgeon General, United States Army, Lieutenant Colonel T. F. Whayne, Lieutenant Colonel G. W. Anderson and Major H. M. Hadock, are naturally those who have been largely responsible for the conception and completion of the undertaking.

*Simmons, J. S., Whayne, T. F., Anderson, G. W., and Hadock, H. M. *Global Epidemiology: A geography of disease and sanitation*. Vol I 504 pp. Philadelphia: J. B. Lippincott Company, 1944.

With the appearance of the three subsequent volumes, which will cover surveys of countries and areas in Africa, Europe, the Near East and the Western Hemisphere, data will be available that should be of incalculable value in the period of global trade and rapid transportation that is certain to follow the termination of war.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BRUCE — Daniel A. Bruce, M.D., of Quincy, died November 5. He was in his eighty-second year.

Dr. Bruce received his degree from McGill University Medical School, Montreal, in 1892. He was a member of the staff of Quincy Hospital for many years, and was a former president of the Norfolk South District Medical Society.

TRASK — Harry W. Trask, M.D., of West Boylston, died November 5. He was in his sixty-fourth year.

Dr. Trask received his degree from the University of Vermont College of Medicine in 1904. He was chief obstetrician at Holden Hospital and school physician in West Boylston many years. He was a member of the American Medical Association.

BOOK REVIEWS

Rehabilitation of the War Injured: A symposium. Edited by William B. Doherty, M.D., and Dagobert D. Runes, Ph.D. 8°, cloth, 684 pp., with 229 illustrations and 17 diagrams. New York: Philosophical Library, Inc., 1943. \$10.00.

Is it possible to make a treatise by bringing together fifty-one essays culled from nineteen current periodicals and two books, American, British and Russian, without delineating the respective fields to be covered and utterly without editorial streamlining? This book does not give an affirmative answer. It contains articles of widely different method and merit, which unfortunately often overlap and equally often leave gaping hiatuses.

The first section, comprising ten essays on neurology and psychiatry, is much the best, as would be expected from the distinction of some of its authors. The section on reconstructive and plastic surgery would be inadequate as an aid to the surgeon confronted by these problems. Several of the topics, such as harelip and cleft palate, have no relation to war injuries, and others are frankly in the field of the beauty parlor rather than that of the military general hospital. In the section devoted to orthopedics, the articles on amputations and limb fitting are useful, but one on leg lengthening seems hardly germane, and the transplantation of the great toe to replace the thumb, "with restoration of all forms of sensibility," by the incredible Russians seems of dubious practical value. Several articles on the organization and administration of rehabilitation centers among the British may prove useful. The next section, consisting of fourteen contributions on occupational therapy and vocational guidance, is marred by the inclusion of much scarcely relevant matter, such as that concerning civilian pulmonary tuberculosis in England. Perhaps the most timely contribution is the last, entitled "Vascular and Neurologic Lesions in Survivors of Shipwreck."

The volume is well printed and bound, but it is impossible to speak so favorably of the illustrations, most of which are miserably reproduced, and many of whose labels can scarcely be deciphered with the aid of a magnifying glass. Furthermore, the proofreading could have been done with more care.

It seems to the reviewer that, although there are many excellent and informative passages in this book, the seeker for guidance in most of the problems that it treats but does not cover will be obliged to turn to other sources.

Hundred Years of Medicine. By C. D. Haagensen, M.D., Wyndham E. B. Lloyd. 8°, cloth, 444 pp., with 42 illustrations. New York: Sheridan House, 1943. \$3.75.

This is an impressively instructive book for the beginning medical student, as well as for the layman. It is absorbing and reflects the judicious attitude of the authors in their effort to trace important medical advances from their origin rather than attempting to survey the whole field of medicine in strict chronological order. Dr. Haagensen, surgeon and pathologist at Columbia University School of Medicine, and Dr. Lloyd, a specialist in public health in England, deal with their material under four sections.

The first section provides the reader with an insight into the state of knowledge that existed a hundred years ago, by scussing briefly the origin of medicine, the theories of medicine in the eighteenth century, the state of hospitals, the military conditions, and the organization and education of the medical profession. The second section, covering medical science during the last hundred years, presents a keen analysis of the germ theory and progress in chemotherapy, vitamin therapy and in knowledge concerning tuberculosis, pernicious anemia, diabetes, diseases of the heart and nephritis. The third section, dealing with surgery during the last hundred years, begins with a discussion of McDowell's ovariectomy and goes on to consider topics such as anesthesia, the conquest of surgical infection, surgical shock, obstetrics and gynecology, orthopedics, neurosurgery, thoracic surgery and radium therapy. The fourth section, concerning the new social aspects of medicine, points out the significance of the ageing of the population since the turn of the century. The authors come to the paradoxical conclusion that although the nineteenth century was one of phenomenal medical progress, the conquests of the diseases of youth that were achieved have left us with health problems even more difficult than those before, — both from the medical and the economic point of view, — namely, the degenerative group of diseases of advancing age, such as heart disease, cancer, cerebral hemorrhage and nephritis. In the final chapter, "The Doctor's Dilemma," the question is raised how best to utilize the vast modern armamentarium of medical knowledge for the benefit of society, and in seeking an answer to this question the authors deal with the challenges offered by the reform in medical education, specialization, the costs of medical care and medical-insurance systems, both abroad and in America. There are forty-two excellent illustrations, a useful bibliography and a good index.

This book should be read by all medical students who wish to gain an appreciation of the facts of disease to which they can attach their fundamental knowledge of anatomy, physiology, pathology and biochemistry. The authors deserve congratulations on an admirable work for the benefit of the layman and the medical profession.

Microscopic Technique in Biology and Medicine. By E. V. Cowdry, Ph.D. 8°, cloth, 206 pp. Baltimore: The Williams & Wilkins Company, 1943. \$4.00.

The purpose of this extraordinarily useful book is "to extend the horizon by exposing in an introductory way a few of the many opportunities awaiting workers in biology and medicine interested in the minute structure of living things." The author, well known as a brilliant scientist, devotes ten pages to a succinct, profitable discussion of choice of methods, as a kind of menu. There follow a few pages on the organization of the laboratory and the standardization of stains. Then, in alphabetical order, come a list of stains, techniques, chemical procedures, apparatus and numerous other valuable items, all briefly discussed and carrying easily available bibliographic references. This book should be a *sine qua non* on the shelves of all medical libraries; its value can only be proved by its constant use.

Blood Supply of the Visual Pathway: A monograph. By Calvin M. Kershner, M.D., M.S. (ophth.). 8°, cloth, 160 pp., with 33 illustrations. Boston: Meador Publishing Company, 1943. \$5.00.

This small monograph attempts to gather together in one place in a systematic manner many of the essential facts

displayed in a wide literature, analyzing and correlating the pertinent information most valuable to the ophthalmologist. The book is divided into two parts; the first covers the general arterial supply and venous drainage, and the second deals with the detailed blood supply and venous drainage of each section of the visual pathway.

There is little about the illustrations to commend them, and the book loses greatly in value from the fact that the author did not include an index.

Human Constitution in Clinical Medicine. By George Draper, M.D., C. W. Dupertuis, Ph.D., and J. L. Caughey, Jr., M.D. 8°, cloth, 273 pp., with 29 illustrations and 30 tables. New York: Paul B. Hoeber, Incorporated, 1944. \$4.00.

Twenty years ago Dr. Draper wrote a book *Human Constitution*. His idea was to apply to clinical medicine the technics of measurement used by anthropologists and in this fashion to study as scientifically as possible the relation of human morphology to disease.

He drew some interesting conclusions from his preliminary work. He thought that certain types of people were likely to develop certain types of disease: the person likely to have gallstones, for instance, was measurably separable from the one likely to develop gastric or duodenal ulcer. He acknowledged that he was describing only the commencement of a program of investigation that he expected to elaborate and stated that eventually he hoped to correlate anthropometric studies on sick people with their physiologic, immunologic and psychologic reactions to such diseases as they were compelled to endure.

This new book is written in collaboration with two other authors, but is in reality an extension of the first. Here, Dr. Draper lays less stress on the methods of measurement employed and much more on psychology. He describes a number of patients constitutionally liable to develop the diseases they proved to have, and through them he attempts to defend further the idea expressed in the first volume, namely, that disease potentially may be a secondary sex characteristic since persons suffering with diseases most commonly encountered in the opposite sex often show constitutional variations approaching the norms for the opposite sex. He carries along his argument ingeniously and graphically. Throughout all his discussion he lays great emphasis on the need in clinical practice for the doctor always to understand how his patients feel and what sort of human beings they are.

The new book was written largely for the benefit of medical students. They will find it readable and stimulating. More mature clinicians will find much in it that is worth while. For underneath a camouflage of newly coined words is repeated a medical truism attributed to old Dr. Parry, of Bath, which, no matter how it is disguised, continues as significant as when it was first propounded: "It is just as important to know what sort of patient has a disease as to know what sort of disease the patient has."

Health and Hygiene: A comprehensive study of disease prevention and health promotion. By Lloyd Ackerman, Ph.D. 8°, cloth, 895 pp., with 59 illustrations and 27 tables. Lancaster, Pennsylvania: The Jacques Cattell Press, 1943. \$5.00.

The author has attempted to provide a book on disease prevention and health promotion "that will appeal to mature, inquiring minds in all circles: nonscholastic as well as scholastic, lay as well as professional, and legal, political, engineering, social service, journalistic, pedagogical and religious as well as medical." This is necessarily a most difficult accomplishment, and it is doubtful whether all these groups will be interested in his efforts. The bibliography is excellent and extensive. The physician might well be interested in this if not in the text. A perusal of the index shows that many diverse phases of medical science are discussed, ranging from the life work of Mary Baker Eddy to penicillin. Some subjects are discussed in detail, others are rapidly reviewed. Diabetes is covered by ten lines, the cancer problem by thirteen pages, and mental hygiene by one hundred and forty-five pages. There is much that could be considered controversial in the work, which makes it challenging

to the interested reader, but those desiring information on certain subjects will be disturbed after reading all sides of the given question to find no solution to the problem. It is definitely not for a casual reader, and although written in an interesting style, the arrangement is such that it requires frequent skipping from one part of the book to another in order to clarify a subject. Public health has largely been omitted. This is so intimately connected with personal hygiene that one would question the omission.

The book is divided into ten sections as follows: "Introduction," "The Evolution of Health Concepts and Health Practices," "The Evaluation and Importance of Health Concepts and Health Practices," "Parasitism and Hypersensitiveness," "Hygiene of the Mouth," "The Hygiene of Nutrition," "Hygiene of the Emotions and the Intellect," "The Hygiene of Mating," "Exogenous Poisons" and "Physical Agents and Their Relations to Health."

Some might wonder why cancer was included under "exogenous poisons," whereas others would question the advisability of including the results of surveys on sex practices in a volume that in the preface is tentatively suggested as a textbook.

NOTICES

SUFFOLK DISTRICT MEDICAL SOCIETY

The fall dinner of the Suffolk District Medical Society will be held on Saturday, November 18, at the Harvard Club of Boston, 374 Commonwealth Avenue, Boston. A social hour beginning at 6:00 p.m. will be followed by dinner in Harvard Hall at 7:15. His Excellency, Leverett Saltonstall, will speak on the topic, "Medical Social Security," and Dr. Roger I. Lee on "Health Insurance?"

It is urged that doctors bring their wives and particularly that the wives of all doctors absent in the service, whether or not the doctor is a member of Suffolk Society, be invited by members as their guests. Each member who sends to the treasurer with his own application the names of such service wives will receive free tickets for them. The tickets, \$3.00 each, must be purchased in advance by sending cash or a check to the treasurer, Dr. Richard S. Eustis, 319 Longwood Avenue, Boston 15. Other members of the Massachusetts Medical Society may apply.

SOUTH END MEDICAL CLUB

A regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 21, at 12 noon. Dr. William P. Murphy will speak on the subject "Vitamins."

Physicians are cordially invited to attend.

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held on Monday, November 20, at 8:15 p.m., at the Boston Medical Library.

The entire program will be devoted to a symposium "Treatment of Subacute Bacterial Endocarditis with Penicillin."

PROGRAM

Experience at the New Haven Hospital. Drs. Jessamine Goerner and Arthur Geiger.

Experience at the Massachusetts General Hospital. Drs. Marion W. Mathews and Paul D. White.

Experience at the Peter Bent Brigham Hospital. Drs. Cutting B. Favour, Charles Janeway, John G. Gibson and Samuel A. Levine.

Experience at the Boston City Hospital. Dr. Maxwell Finland and associates.

Experience at the House of the Good Samaritan. Drs. Benedict F. Massell and Mary Meyeserian.

Discussion. Dr. Chester S. Keefer.

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Harvard Club on Friday, November 17. There will be an x-ray conference at 4:30 p.m. 8:00 p.m. the following program will be presented:

Pulmonary Infarction.

Roentgenologic Appearance. Dr. Laurence L. Robbins
Clinical Features and Treatment. Dr. Robert R. Lint
Intrapulmonary Lymphatic Spread of Metastatic Carcinoma.

Roentgenologic Appearance. Dr. H. Peter Mueller.
Pathology. Dr. Ronald C. Sniffen.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The sixteenth annual meeting of the New England Obstetrical and Gynecological Society will be held at the Harvard Club of Boston on Wednesday, December 6.

AUSTEN RIGGS FOUNDATION

The Austen Riggs Foundation Medical Advisory Board commemorating the twenty-fifth anniversary of its hospital by holding the annual meeting this year at the Academy of Medicine in New York City on Wednesday, November 21 at 3:30 p.m. Dr. Lawrence S. Kubie will present a paper on the problems of brief psychotherapy and the training of therapists, particularly the role of the small sanitarium at hospital in such a program. A discussion will follow by Brigadier Rees, of London, the Salmon Lecturer, Major General Chisholm, of Ottawa, and others.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for candidates will be held in various cities of the United States and Canada and by special arrangements at Army and Navy stations on Saturday, February 3, 1945, at 2:00 p.m. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications for this year's examinations must be in the office of the secretary by November 15, 1944.

Arrangements will be made, so far as is possible, for candidates in military service to take the Part I examination (written paper and submission of case records) at their places of duty, the written examination to be proctored by the commanding officer (medical) or by a medical officer designated by him. Material for the written examination will be sent to the proctor several weeks in advance of the examination date. Candidates in military service who wish to do so may send their case records in advance of the examination date to the office of the secretary. All other candidates should present their case records to the examinee at the time and place of taking the written examination.

The Office of The Surgeon-General of the United States Army has issued instructions that men in service eligible for Board examinations be encouraged to apply and that they may be ordered to detached duty for the purpose of taking these examinations whenever possible. The Office of The Surgeon-General of the United States Navy presumably takes a similar attitude on this matter.

The place of the Board's Part II examination in May or June, 1945, has not yet been decided, but it is likely to be held in that city nearest to the largest group of candidates. The exact time and place will be announced later.

If a candidate in service finds it impossible to proceed with the examinations of the Board, so that his plans are thus interrupted, deferment of parts of these without time penalty will be granted under a waiver of the published regulations covering civilian candidates.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

(Notices continued on page xv)

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PRIMARY ATYPICAL PNEUMONIA OF UNKNOWN ETIOLOGY*

SVEN GUNDERSEN, M.D.†

HANOVER, NEW HAMPSHIRE

In the United States and in many other regions throughout the world from which adequate medical reports are available, there appears to have been, during the last few years, an increased incidence of an unusual form of pneumonia, the etiology of which is unknown. It has been refractory to the methods of treatment specific for bacterial pneumonias.

Many papers on this subject have appeared in the recent medical literature. In a thorough review published in the *Journal* about two years ago, Finland and Dingle,¹ in addition to summarizing the clinical, laboratory, x-ray and pathologic features of the disease, emphasized certain other points. They state that this is probably not a new disease, inasmuch as a description of a closely similar malady dates back seventy-two years; that the etiology is unknown and that it is therefore unwise to assume that the etiology is a virus; that as a result the diagnosis is likely to be at best uncertain; and that most etiologic studies seem to exclude any relation of the disease to other forms of pneumonia of known virus etiology, such as ornithosis — including psittacosis — and influenza. Such studies, furthermore, show that the disease probably bears no relation to Australian or American Q fever, or to similar diseases with pneumonic lesions of rickettsial etiology. It is quite possible that several etiologic agents are involved, and that therefore so-called "virus pneumonia" is a syndrome rather than a true entity. For this reason, it becomes all the more important to analyze carefully and become thoroughly acquainted with the clinical and laboratory features as they are revealed at present.

Primary atypical pneumonia has been described in most studies as having influenzalike symptoms, often associated with evidence of mild upper respiratory infection, few physical findings, which are usually slow in making an appearance, and variable but disproportionately extensive lesions as shown by x-ray examination. Other laboratory tests have

been inconsistent and disappointing. Periods of fever and disability have generally been long, making the illness of considerable economic importance.

Complications and sequelae have been described as mild and trivial. Deaths in most series have been absent or very few. In the scarce reports of cases that have come to autopsy, patchy, hemorrhagic, interstitial bronchopneumonia, associated with acute bronchitis and bronchiolitis, has been found. Areas of atelectasis and emphysema with small patches of red or gray consolidation have been described. The main microscopic feature has been a hemorrhagic or mononuclear-cell exudate in the alveoli. No inclusion bodies have been noted.

A few of these cases began to appear at the Hitchcock Hospital and the Dartmouth College Infirmary in 1938, but by far the largest number have been seen there in the last two and a half years. The naval officers of the first indoctrination school were particularly often afflicted. Many cases in children and adolescents have come from summer camps. Excellent opportunity for close observation and study has been afforded in this group of patients because all of them have been hospitalized where x-ray and laboratory facilities could be freely used. All have been under the care of five physicians who have special interests in internal medicine or pediatrics.

From January, 1942, to February, 1944, inclusive, 162 patients with a final diagnosis of primary atypical pneumonia were in the hospital. In all of them there was a confirmation of the diagnosis of some sort of pneumonia by x-ray examination. Only 122 cases, however, including 3 fatal ones, 2 of which came to autopsy, were used for analysis in this study. The 40 rejected cases were considered unsuitable for various reasons. Sputum tests were inadequate in most of them; the clinical records were incomplete in a few; and some were doubtful cases, in which the pneumonia, on more detailed consideration, seemed likely to be bacterial or to be a complication of some other disease.

One hundred and eight of these 122 patients (88 per cent) were males. This percentage is not in

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 16, 1944.

†Instructor in physical diagnosis and medicine, Dartmouth Medical School; member of staff, Mary Hitchcock Memorial Hospital and Hitchcock Clinic.

accord with that of other reports and is probably explained by the high incidence of males in the community at the time. These men were living in crowded quarters and going through training that was strenuous and unusual. The youngest patient was three years old and the oldest seventy-nine; 101 patients were in the second or third decade of life. This is in keeping with other studies, which indicate that adolescents and young adults are particularly susceptible to this malady, in spite of the fact that there was a special age selection in this college community. The age incidences by decades were 2 in the first, 60 in the second, 41 in the third, 12 in the fourth, 4 in the fifth, and 1 each in the sixth, seventh and eighth.

Many of these patients were seen in the summer and fall of 1942, and even more in the winter of 1942-1943. It is interesting to note that no patient was admitted to the hospital in May or June of either year. The period of observation is too short to permit any conclusions, but there is at least a suggestion that the seasonal incidence is quite different from that of diseases due or related to the hemolytic streptococcus. The monthly incidence (Table 1)

TABLE 1. Monthly Incidence.

MONTH	1942	1943	1944
January	1	17	5
February	3	6	1
March	3	10	
April	2	1	
May	0	0	
June	0	0	
July	4	1	
August	8	1	
September	11	0	
October	9	4	
November	16	5	
December	14	4	

coincides closely with that in a series reported by Murray² from the Department of Hygiene, Harvard University.

The period of hospitalization varied from six to sixty-seven days, with an average of nineteen days. This was due in part to the fact that the patients in military service, of which there were many, had to be well along in convalescence before they could be dismissed.

The febrile period during hospitalization varied from one day to twenty-eight days, with an average of nine days. This average is a little higher than that of cases of pneumococcal lobar pneumonia in which the patients recover spontaneously without specific serum or sulfonamide therapy.

In reviewing the symptoms of these patients (Table 2), a few striking points became evident. Cough, headache, malaise and sore throat were the most frequent symptoms, in the order named. Shaking chills were relatively infrequent. Cough was often slow in development. In most cases it was explosive, hacking and distressing; in the average case it gradually became productive of small amounts of mucopurulent sputum. Of great im-

portance for the differential diagnosis was the complete absence of typical pleuritic pain and of "prune juice" or rusty sputum. Numerous other complaints were offered by a few patients, as indicated in the table. Dyspnea occurred in only 2 cases, but in both there was a fatal outcome.

The term "atypical pneumonia" is particularly appropriate in relation to the question of physical findings. Most patients had few signs and a minor

TABLE 2. Distribution of Symptoms

SYMPTOMS	NO. OF CASES
Cough	114
Headache	71
Malaise	58
Sore throat	50
Chills or chilliness	44
Coryza	32
Appreciable amount of sputum	27
Substernal ache (or tightness)	12
Fatigue	11
Anorexia	9
Aching eyes	8
Fever	7
Vomiting (or nausea)	5
Hoarseness	3
Dyspnea	2

proportion showed none whatever. Typical signs of consolidation were detected in less than one tenth of the patients, and came late in the course of the disease. Rales, either crepitant or musical, particularly after cough, were detected in 103 cases, but again usually appeared late. There was dullness in 34 cases, and increased vocal fremitus in 8. The breath sounds were diminished in 23 cases and otherwise changed in 11. It is worth emphasizing that no undoubted pleural friction rubs were felt or heard, nor was there ever any convincing evidence of collection of fluid in the pleural cavity. Generally speaking, most of the patients did not look particularly ill at any time, even when they had high fever. Usually, the pulse was relatively slow. Rarely was there cyanosis or abdominal distention. Herpes simplex was not reported. Slight to moderate inflammation of the nares and pharynx was apparent in most patients. The spleen was palpable for a few days in 2 cases.

The sputum was examined in every case, either by culture and typing of any pneumococci that could be isolated or by the gram-staining of smears followed by direct typing of the sputum if organisms morphologically resembling pneumococci were seen. Eighty-two cases showed many organisms in the cultures with no one of them predominating; the mixtures consisted chiefly of green-producing streptococci, staphylococci, pneumococci, *Micrococcus catarrhalis* and influenza bacilli. Hemolytic streptococci were present in 6 cases, usually in small numbers. Typable pneumococci were found in small numbers in only 4 of 77 cases examined for this purpose; these were types 3, 4, 8 and 23, respectively.

Blood cultures were done in 55 cases, and were reported as sterile in all but 1, in which contamination was suspect

The white-cell counts ranged from 3000 to 23,000. The average count was higher during the latter part of the febrile period than at the beginning of the illness or at the end of the period of hospitalization. The percentage of polymorphonuclear leukocytes averaged 77, and in most of the severely ill patients there was an increase in immature forms — in 1 case to 35 per cent.

Sulfonamides were given as a therapeutic and diagnostic test in 63 cases in adequate dosage, as judged by blood-level determinations, without any notable beneficial effect on the symptoms, fever or time of hospitalization. Fifty-eight of these patients received sulfadiazine, 4 sulfathiazole, and 1 sulfamerazine.

Complications and associated diseases occurring during the convalescent period were relatively few and mild. Sinusitis developed in 4 cases. Otitis media, chiefly catarrhal, occurred in 5 cases, and in all of them was successfully treated by x-ray therapy and other conservative measures. One patient — a child — with the symptoms and signs of meningitis had increased cells in the spinal fluid, chiefly lymphocytes, but no organisms could be isolated by smears or culture, and the clinical condition improved rapidly. There was mild jaundice in 1 case, and measles in 1.

Bronchiectasis as a late complication was proved by a lipiodol bronchogram in 1 case and was suspected in a second. Follow-up study of the latter case proved impossible because the patient was transferred to a Navy hospital.

As stated previously, the diagnosis of pneumonia was confirmed by x-ray examination in all cases. The right lung was involved in 54 cases, the left in 44, and both lungs in 24. The site of involvement was the lower lung field in 90 cases, — particularly at the cardiophrenic angle, — the middle lung field in 29, and the upper lung field in 13. The entire lung field was involved in 5 cases. Patchy areas of infiltration with indistinct borders were considered the most typical picture, but several cases of distinctly lobar consolidation were seen. Accentuation of the lung markings, giving a streaked appearance of the involved area, was more pronounced than it is in most cases of bacterial pneumonia. A few of the x-ray films, taken separately and without regard for follow-up study, could easily have been interpreted as indicating pulmonary tuberculosis. Many cases showed the most extensive changes when the general condition of the patients had been improved for several days.

In addition to providing bed rest, good nursing care and adequate intake of fluids and salt to combat unusual loss from sweating, which was often excessive, the main efforts in treatment were directed toward relief of the most annoying symptoms. Inhalations of steam, expectorants containing iodine, and codeine afforded the best relief from cough, especially in the early stages. Salicylates, with or

without codeine, gave fair relief from headaches. Hot gargles or irrigations of saline or weak perborate solutions were frequently used for sore throats. Two of the 4 patients with sinusitis were successfully treated by the usual simple measures, but the other two required displacement procedures. Administration of increased concentrations of oxygen was rarely necessary; its use was disappointing in the patients who needed it most — namely, those with dyspnea and cyanosis. There appears to be no specific therapy for atypical pneumonia. Favorable reports of the use of x-ray treatment and of blood transfusions from convalescent patients have appeared, but we have had no experience with these measures.

The three fatal cases require special consideration, and are described in the following reports.

CASE 1. C. T. B. (D.H.H. 5587), a 19-year-old college student, entered the infirmary on March 21, 1942, with a 24-hour history of chilliness, cough, sore throat, malaise and discomfort in the midchest anteriorly. He had been dismissed from the infirmary 8 days previously, after a stay of 17 days, having made a good recovery from infectious mononucleosis, which was typical from both clinical and laboratory standpoints. The rest of the history was not remarkable.

Physical examination soon after admission showed few signs in the chest, but x-ray examination of the chest on the day of admission showed irregular mottling in the right base. Dyspnea, although not apparent in the first 3 days, gradually became more distressing until death 10 days after entry. This was associated with cyanosis and was not relieved satisfactorily by an oxygen tent that was used continuously for the last 7 days of the illness.

The white-cell count varied from 6000 to 12,000, with 37 to 85 per cent polymorphonuclear leukocytes. During the last few days the percentage of immature cells increased to 31 per cent. The sputum showed mixtures of organisms but no hemolytic streptococci or typable pneumococci. Two blood cultures showed no growth.

Sulfadiazine given in adequate doses for the first 3 days was ineffective. Two additional x-ray examinations showed increased consolidation in the base of the right lung and a spreading lesion in the left hilar region. Dr. Donald S. King, of Boston, who saw the patient in consultation 2 days before the fatal outcome, agreed with the diagnosis and therapy and suggested that the poor response was possibly due to the blood changes resulting from infectious mononucleosis. Death was preceded for 4 days by an agitated delirium. Permission for autopsy could not be obtained.

CASE 2. E. C. D. (A 27,848), a 79-year-old retired printer, entered the hospital on November 3, 1942, with a 3-day history of cough and chills. He had made a good recovery from pneumonia 8 months previously. Otherwise the past history was irrelevant.

In addition to a clouded mental state and a distended, tympanitic abdomen, examination revealed labored breathing and patchy signs of consolidation in both lungs, confirmed by x-ray examinations. There was no improvement with sulfadiazine. The respirations became more rapid and labored in spite of the use of an oxygen tent, cyanosis appeared and became more marked, and the patient died 6 days after admission.

The white-cell count varied from 6000 to 9000, and a single differential count showed 81 per cent polymorphonuclear leukocytes. A blood culture was sterile, and only untypable pneumococci were present in the sputum.

Autopsy. The main findings were extensive, patchy areas of gray and red consolidation in both lungs, much frothy, gray-red fluid and purulent material exuding from the bronchi, 1000 cc of clear fluid in each pleural cavity, dilatation of the heart and moderate portal cirrhosis of the liver. Microscopically, the lungs showed scattered areas in which the alveoli were filled with pale, pink material; other areas contained

polymorphonuclear leukocytes and large, pigment-filled macrophages. The pathologists considered these findings consistent with virus pneumonia.

CASE 3. H. B. (A 330), a 38-year-old man, was admitted to the hospital on December 22, 1942. He had suffered from asthma for a long time and was an alcohol addict. For 7 days before entry he had complained of chills, malaise, headache, productive cough and dyspnea. Sulfadiazine had been given before admission, without improvement.

Physical examination showed euphoria, dyspnea, rapid respirations, widely scattered rales and signs suggesting consolidation at both bases—confirmed by x-ray examination. The patient's condition deteriorated gradually in spite of oxygen therapy and other supportive measures, and he died 8 days after admission following a 3-day period of coma.

The white-cell count increased from 7000 to 14,000, with 75 to 94 per cent polymorphonuclear leukocytes and 22 per cent immature forms. The sputum showed a mixture of organisms, including untypable pneumococci. No blood culture was done.

Autopsy. There were patchy areas of consolidation in both lungs, much gray-green, tenacious material in the bronchi, enlargement of the hilar lymph nodes and punctate red areas in the white matter of the cerebrum, internal capsule and the middle and superior cerebellar peduncles. Histologically, all regions of the lung revealed marked congestion of the alveolar capillaries. Some alveoli were filled with pink, amorphous material and others had interlacing strands of fibrin. The most characteristic appearance was that of masses of large macrophages filling the alveoli. Areas of necrosis were frequent. In some sections fibroblasts were growing into the alveolar exudate. Other findings were acute hemorrhagic encephalitis and petechial hemorrhages of the kidneys.

SUMMARY

Primary atypical pneumonia is discussed, particularly in the light of experience with 122 closely observed cases in a twenty-six-month period.

Certain points in differential diagnosis are emphasized, with special reference to symptoms, signs, and x-ray findings.

A case with bronchiectasis as a late complication is reported.

The clinical features of 3 fatal cases and the pathologic findings of 2 autopsied cases are described in detail.

REFERENCES

1. Finland, M., and Dingle, J. H. Virus pneumonias associated with known non-bacterial agents, influenza, psittacosis and Q fever. *New Eng J Med* 227:342-350, 1942.
2. Murray, M. E., Jr. Atypical bronchopneumonia of unknown etiology possibly due to filterable virus. *New Eng J Med* 222:565-573, 1940.

DISCUSSION

DR. R. C. BATT, Berlin: I have had 2 cases of atypical pneumonia in the last year, and one of them was mistakenly

diagnosed as tuberculosis, without adequate findings. It is extremely important to take roentgenograms of the chest, but it is also important not to lose track of the clinical picture of the picture. In the case just mentioned there was involvement of the right upper lobe and a suspicion of cavities. It is impossible to distinguish by x-ray examination between atypical pneumonia and tuberculosis, but this differentiation is very important, and Dr. Gundersen has shown how to make it.

I should like to know whether Dr. Gundersen considers night sweats typical of this disease.

DR. R. W. ROBINSON, Laconia: I should like to ask Dr. Gundersen whether he has come across a complication such as we have had in 3 cases that were diagnosed as influenza infection. For some weeks before admission to the hospital, and at that time also, all had symptoms of pleuritic pain. X-ray examination showed what appeared to be massive fluid—in 2 cases on both sides of the chest and in 1 on one side—but tapping failed to produce fluid. Six weeks later in all 3 cases there was evidence of a localized empyema, which was opened. The organism in each case was a staphylococcus. All the patients ran a clinical course that was identical with that of Dr. Gundersen's patients. The blood pictures were also identical; that is, the white-cell count was never above 9500.

I am wondering whether pleuritic infection is a frequent complication of atypical pneumonia.

DR. C. L. SMART, Laconia: What does Dr. Gundersen think of x-ray treatment in this type of pneumonia?

DR. GUNDERSEN: In answer to Dr. Batt's question about night sweats, I have no figures for this series, but I am sure they were extremely frequent, and they are hard to handle. For this reason, many physicians are opposed to using salicylates for this disease, because they simply make the situation worse. Of course, the sweats occurred irregularly in many of these patients, coming both during the day and at night. As shown by one of the clinical charts, the fever is most irregular, dropping at any time of the day or night.

I have come across reports of pleurisy and empyema as a complication of this disease, but have not been much impressed with them, because these complications have always been due to pyogenic invaders that have been considered secondary to the atypical pneumonia. In a recent report of some 700 cases (Owen, C. M. Primary atypical pneumonia: analysis of 738 cases occurring during 1942 at Scott Field, Illinois. *Arch. Int. Med.* 73:217-231, 1944), a small percentage of patients with fluid, mostly sterile, was mentioned.

In answer to Dr. Smart's question about x-ray therapy, he may have in mind Dr. Oppenheimer's experience. I have studied Dr. Oppenheimer's report, and for all I know this may be a valuable method of treatment. We have had no experience with it. Certainly Dr. Oppenheimer's reported results suggest benefit, particularly if x-ray treatment was used in the first week or two weeks, and particularly if very small doses were given. I believe, however, that any form of therapy is extremely difficult to evaluate in a disease of this sort, when one cannot even be sure that he is dealing with a clinical entity. There may be many etiologic factors or agents that are responsible for this picture.

NATIVE MEDICAL PRACTICES IN THE SOUTHWEST PACIFIC

RAYMOND A. DILLON, M.D.*

BOSTON

THE small atolls of the Gilbert and Ellice Islands are practically the only remaining places in the South Seas where the grass skirt and the uncovered breast have not come under the white man's ban. Baths are frequent and the natives are clean. It is refreshing to get away from the usual greasy, dirty, ragged Pacific "Mother Hubbard," with its long sleeves and high neck, so out of place in a steamy climate.

In the Pacific was once the most perfect quarantine against disease ever known — cannibalism. Anyone — disease carrier or not — who strayed to another village was eaten. Social intercourse was reduced to a minimum. If an epidemic broke out in a locality, everyone either died or recovered. The disease did not spread from village to village or island to island as it does today.

In general, there are three types of native treatment: surgery, cautery and massage. Various charms of one kind or another are also extensively used against disease. Conversations with many of the older members of the population indicated that herbal medicines have never been employed, except for the oil of the coconut, which was, and still is, used as a purgative. Its properties are closely similar to those of castor oil. It is obtained by squeezing copra — the dried meat of the ripe coconut.

Every year a great many natives die of pneumonia, owing to the practice of treating a fever by sitting for hours immersed to the neck in cold sea water. In spite of crowded conditions and the centuries-old threat of overpopulation, there is little intestinal disease, owing to the strictly enforced custom of depositing human waste in the sea.

Cauterization of the skin is accomplished by the application of the glowing end of a smouldering torch, made of strips of rags or bark rolled into a cylinder half an inch in diameter. It is applied for about a second. In treating a disorder, the cautery is rarely applied to the actual area of pain, but usually at points above and below it. In abdominal pains, the application is made in a circle, using the umbilicus as a center.

Massage takes the form of pressing, pinching, manipulation, friction and rubbing, but the skill of the natives in this area does not approach that of the Samoans. Massage is principally used to strengthen weakened or stiffened muscles.

Fractures are bathed in hot water and wooden splints are applied. Massage is begun early.

An injured eye is treated with the steam coming from a coconut shell half filled with water into

which heated pebbles have been dropped. Another method is for the doctor to lick the eyeball with the tip of his tongue.

Throughout this part of the world, before the advent of the white man's trading schooner, cutting implements were obtained, of necessity, from whatever materials were locally available. Obsidian, which can be fashioned into knives, axes and arrowheads, is found on some of the volcanic islands. Bamboo has a sufficiently keen edge, when split, to perform such minor operations as circumcision, which is only a dorsal slit. Formerly a sharp-edged shell was often used, but now a favorite instrument is an old safety-razor blade.

On the true coral atolls, which make up the Gilbert and Ellice Islands, bamboo does not grow and there are no volcanic stones, all sand, stone and soil being of coral origin. On some of these islands, it is said that the umbilical cord was usually cut with a sliver of bamboo found on the beach, which had drifted in from the sea. Scrapers and axes are made from fragments of shells or the carapace of turtles, but this kind of material is useless for surgery. For this purpose, the razor-edged teeth of sharks are used. Excellent lancets are made by binding a tooth to a wooden handle 10 inches long and of the diameter of a fountain pen. A number of these teeth lashed to a club make an effective weapon that has been used by these warlike people for centuries.

When a shark is caught, the jaws are removed and dried in the sun. The teeth become loosened when soaked in fresh water, after which they are extracted and kept in a small coconut-fiber bag until needed. The teeth from the upper jaw have a saw-toothed edge and are used in making long incisions, whereas the smooth-edged ones from the lower jaw are used for puncturing the skin, as in bloodletting. The lances are called *ponga*. In use, the lance is held in the left hand so that the point of the tooth is over the spot to be punctured, and the point is driven in by tapping the handle with a mallet ten inches long held in the right hand. Long incisions are made by holding the lance at such an angle that when it is tapped only the front edge of the tooth cuts. The blade is then moved forward and the procedure repeated, the result being a clean incision. This kind of incision is used for removing lipomas, tuberculous lymph nodes, leperous tissue, elephantoid scrotums and the like.

In removing a subcutaneous tumor, such as a lipoma or enlarged tuberculous node of the neck, an assistant, holding a rectangular piece of turtle carapace in each hand, presses downward and inward on either side of the mass so that it is compressed and raised above the surrounding parts. The in

*During 1940 and 1941, Dr. Dillon spent eighteen months with an expedition exploring the lesser-known island groups of the Pacific.

cision is made straight across the top of the tumor in the manner described above, and the distended skin falls apart, exposing the tumor. Owing to compression, there is little bleeding until the pieces of turtle shell are removed, when the assistant attempts to remove the blood by blowing. The tumor is drawn out of the wound by a pearl-shell fishhook or a forklike piece of wood while the surgeon frees it from the underlying tissues. The wound is usually covered with soft strips of beaten coconut husk, bound in place with strips of pandanus leaf, such as are used in making mats. The skin edges are held in apposition by pressure, no sutures being employed.

This method is employed to remove the painful sores of yaws on the soles of the feet, which occur principally in the young. They are completely excised. In the Solomon Islands, this is accomplished by thoroughly scraping out the affected tissue with the fingernail.

In the Southwest Pacific the incidence of yaws is almost 100 per cent, and that of filariasis is extremely high. The crude surgery described above is often used to remove large scrotums found when elephantiasis develops, the hypertrophied tissue being excised after the testicles have been pushed back with the fingertips.

A *ponga* with a long, thick tooth is used for the removal of hydrocele fluid and for bloodletting. In puncturing the scrotum, injury to the testicles is avoided by holding it so that the liquid distends the bottom of the sac, at which point it is incised. In the Tonga Islands, hydrocele is sometimes drained by using a piece of hollow bone from a cooked bird as a cannula.

For bloodletting, the point of the instrument is driven into a distended vein on the anterior surface of the arm. Just what the native indications for venesection are I was unable to determine.

For opening boils or filarial abscesses, a moderately broad tooth with a smooth edge is used. This is done by driving the blade into the abscess with a single sharp blow. At sea, in a small sailing vessel, boils are a frequent affliction. I made use of this rather crude native instrument, after sterilization by boiling, and found it very effective and as painless as any method I know of.

One instrument, with a small, fine-pointed tooth, is used to make small puncture wounds over gum-boils, swollen areas and bruises. In the case of headache or muscle ache, the needlelike point is gradually moved over the whole area of pain while the lance is tapped rapidly and lightly.

In the New Guinea area, I was amazed to hear that the tribal doctor, to cure a headache, shot the patient in the head with a bow and arrow. Investigation revealed that the bow was a miniature one with just enough force to cause a needlelike arrow to draw a tiny drop of blood. A number of these small punctures were made over the aching area.

The end result was essentially the same as in the Gilberts.

As throughout most of the Pacific area, there is no objection to autopsies. The natives often do post-mortem examinations on their close relatives when there is doubt as to the cause of death.

The midwives are respected members of the community and receive payment in the form of food and fine mats for their services. Because of this there is considerable incentive for them to become as skillful as possible. A midwife is visited at about the fifth or sixth month of pregnancy, at which time massage of the abdomen, consisting of a clockwise motion over the uterus, is given twice weekly. This is supposedly done to turn the fetus and assure correct presentation, but there is probably also the intention of producing abortion. This latter is attempted by massage with heavy pressure on the abdomen and by having the patient lie with a heavy stone resting on the abdomen. Another method is to strike the back just below the kidney region with the side of the hand. These methods are quite inefficient, as indicated by the large number of illegitimate children and by the prevalence of widespread infanticide in former times. In some of the islands there were rumors that abortion was produced by potions made from various herbs, but further information could not be obtained. Apparently this is a modern practice, because internal medicine was probably not used in the past.

Superstition plays a large part in the routine of the pregnant woman. She cannot eat while walking on the road for fear the child will beg. She cannot chew the doubled-bodied pandanus fruit for fear of giving birth to twins, and she is not allowed to cut her food with a knife for fear the child will have a harelip.

The midwife is sent for when labor pains begin. The patient takes her place on a bed of mats prepared especially for the occasion. The position adopted during delivery differs among the various localities, the most frequent being the supine one, with the legs bent at the knees. Another is much the same as Sims's position. Often, however, the patient simple squats. The abdomen is massaged, and after the placenta has come away, the cord is tied with a strip of leaf of the pandanus plant. It was formerly severed with the sharp edge of a clam-shell. The orifice of the vagina is smeared with oil and covered with breadfruit leaves, held in place by a T belt of plaited fibers. This pad is removed and a new coating of oil is applied as often as necessary. The placenta is usually buried, with a coconut planted over it.

If the infant does not begin to breathe spontaneously, both the nose and mouth are sucked to remove mucus, and air is blown into the ears and nostrils. Before the cord is cut the placenta is placed in a vessel of hot water and mouthfuls of cold water are squirted over the infant's face.

For the rare cases of puerperal infection, the treatment is massage of the abdomen. This seems to be the usual treatment throughout the Pacific. Once on a visit to lonely Pitcairn, I was told of a patient who had died a few days previously, and was asked how treatment could have been improved. The mother, after giving birth to twins, had had her uterus washed out with an unsterilized fountain syringe from which a large part of the population had recently received enemas. The resulting infection was vigorously treated by massage.

Until the breast supply of milk becomes available, the newborn is given coconut milk, which appears to be adequate. The child is fed at the breast so long as the supply lasts, usually about eighteen months. When the breast becomes unavailable, the child is fed the soft, almost jellylike meat in the interior of the young coconut, beautifully carved spoons of mother-of-pearl being used.

I always enjoyed watching a baby being bathed. This was accomplished very simply by the mother's

holding the infant up in front of her and squirting mouthfuls of water on it.

At Tarawa was the medical center of the Gilberts. Dr. K. R. Steenson had a small hospital consisting of sixteen individual huts. Unassisted, he was trying to look after the health of 45,000 people living on hundreds of tiny atolls spread over a thousand miles of water. He is well trained and well read and a dynamo of energy. Because of the war no new supplies had reached him for a long time and he was using coconut fiber as a suture material. I saw several cases in which this had been used, and the results were excellent. Dr. Steenson is now a prisoner of the Japanese.

I should like in closing to pay tribute to the hard-working physicians of the remote islands of the Pacific. Not once did we run across the "beach-comber doctor" so universal in fiction and the theater. All were able, kind, well trained and doing splendid work against great odds.

A SIMPLIFIED METHOD FOR CULTURING FUNGI FROM THE SCALP*

ERNST BERNHARDT, M.D.†

BOSTON

LIVINGOOD and Pillsbury¹ state, after reviewing the recent American literature, "Ringworm of the scalp cannot be intelligently treated without cultural diagnostic methods." Although it is generally easy to distinguish microsporiasis, trichophytosis and favus from each other by microscopic examination, the statement quoted seems correct, since it may be difficult clinically to distinguish tinea capitis infections with *Trichophyton gypseum* (*mentagrophytes*) from infections with a *Microsporum*. Furthermore, it is impossible to decide clinically whether *Microsporum audouini*, *M. canis* (*lanosum*) or *M. gypseum* (*M. fulvum*) is involved. Cultural diagnostic methods permit the differentiation of the four species mentioned, which is important particularly for *M. canis* and *M. audouini*. These fungi are nearly exclusively the causative agents of tinea capitis in this country. Infections with *M. canis* do not require x-ray treatment, and the search for the ultimate source of infection must be directed to an animal. If *M. audouini* is found to be the causative agent, the patient's classmates and playmates should be examined under a Wood's light; x-ray depilation seems indicated for children too young to expect pubertal changes soon, and not improved after four weeks of less energetic treatment.

Cultural diagnostic methods would probably be used more frequently if they were available at low cost and without special equipment. The present paper reports a method that can be readily performed with little expense at the physician's office and permits the differentiation of the microsporum fungi from each other and from *T. gypseum*.

The most practical formula for the culture medium was found to be as follows:

Rice.....	5 cc.
Water.....	25 cc.
Aqueous 1:10,000 solution of gentian violet†.....	0.8 cc.

The only equipment required consists of a saucepan, 100-cc. or 125-cc. bottles, a 1-cc. pipette or syringe, test tubes, a platinum loop or needle and a microscope.

For the preparation of the medium a test tube marked at the 5-cc. level and another at the 25-cc. level serve as measures. The 1:10,000 gentian-violet solution is made up by adding 1 cc. of a 1 per cent. alcoholic or aqueous solution to 99 cc. of water. The rice is placed in a bottle of 100-cc. capacity and is washed with water, which is changed three times after thorough shaking. The exact amount of water and the gentian-violet solution are then added. The bottles are plugged with nonabsorbent cotton and are heated in boiling water for thirty

*From the Department of Dermatology and Syphilology, Beth Israel Hospital.

†Assistant in dermatology and syphilology, Beth Israel Hospital, graduate assistant in dermatology, Boston City Hospital

†The gentian violet used in these experiments was a brand called Proctanin, manufactured by Merck and Company, Incorporated, Rahway, New Jersey.

cision is made straight across the top of the tumor in the manner described above, and the distended skin falls apart, exposing the tumor. Owing to compression, there is little bleeding until the pieces of turtle shell are removed, when the assistant attempts to remove the blood by blowing. The tumor is drawn out of the wound by a pearl-shell fishhook or a forklike piece of wood while the surgeon frees it from the underlying tissues. The wound is usually covered with soft strips of beaten coconut husk, bound in place with strips of pandanus leaf, such as are used in making mats. The skin edges are held in apposition by pressure, no sutures being employed.

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reциably alter the character of the colony or the rate of growth of either fungus. A high percentage of water was used to keep the medium fit for inoculation for more than a month. Ordinary medicine bottles withstood the flaming of their mouths without cracking.

The addition of gentian violet to the medium is necessary to permit simplified sterilization. In a small series of experiments some bottles were found to be contaminated when gentian violet was omitted, but in more than one hundred sets of sterilizations the medium containing gentian violet remained sterile.

The primary colony of *M. canis* appears on gentian-violet rice in a few days. It is covered by aerial hyphae forming a white, cottony growth. The base of the colony soon becomes yellowish. After the colony has grown for a few days, microscopic examination reveals numerous, thick-walled spindle spores (fuseaux) with pointed ends containing when fully developed five to twelve well-defined compartments. The outside of these spores is covered with all excrescences (Fig. 1A).

First cultures of *M. audouini* become visible after two weeks. They lack aerial growth. The colony is characterized by a slightly brownish discoloration spreading at the rate of about 1 cm. a week over the entire surface and throughout the medium. Daylight shows the discoloration earlier than does artificial light. Microscopic examination of smears from the discolored area shows delicate, curved and branched mycelial threads but never spindle spores (Fig. 1B). Comblike formations, quiet mycelia and single chlamydo spores are occasionally found.

Colonies of *M. gypseum* develop a white, cottony aerial growth. The central area of their surface soon turns to light cinnamon. Microscopically numerous spindle spores with four to six compartments are found (Fig. 1D).

The early colonies of *T. gypseum* are covered with white, cottony, felty or powdery growth. After a few days of growth, microscopic examination reveals innumerable spherical or ovoid microconidia, about 2 microns in diameter. During the second week spirals may also be seen (Fig. 1C).

The primary colony of *Achorion schoenleinii* fails to develop aerial mycelium. It is differentiated from that of *M. audouini* by its yellow or orange color and its slower spread, which scarcely exceeds 1 mm. a week (subcultures grow more rapidly). Microscopically, large chlamydo spores are seen in colonies a few days old.

Fourteen strains of *M. canis* were isolated on gentian-violet rice. One isolation failed at the first attempt because of a greenish contaminant, which

also developed on Sabouraud medium. Hair stumps from the same material were covered with 90 per cent alcohol and inoculated after its evaporation; pure cultures then developed on each medium.

Seven strains of *M. audouini* developed on the first attempt on gentian-violet rice. There were enough hair stumps left of most samples to repeat the cultures equally successfully after weeks or even months.

In some cases hair stumps from diagnosed cases were used for culture after the patients had received topical medication. In one of these cases *M. audouini* failed to grow on either gentian-violet rice or Sabouraud medium. Fungicides were supposed to be responsible for this failure. One strain of *M. canis* from a treated patient failed to grow on Sabouraud medium but developed on gentian-violet rice.

The reported experiments show isolation of the fungi usually responsible for tinea capitis to be as successful on gentian-violet rice as on Sabouraud medium. Their features differ widely enough on the former to distinguish them from each other. These statements seem conclusive at least for *M. canis* and *M. audouini*, since fourteen and seven strains of these fungi, respectively, were isolated, numbers not exceeded in the reports of authoritative authors^{2,3} when testing a new or modified culture medium. Other species of *Microsporum* are rarities in this country. If encountered, they may be identified with the help of Conant's² taxonomic study on a polished-rice medium.

The disadvantage of the gentian-violet rice is that Sabouraud medium frequently permits a diagnosis of *M. audouini* at an earlier date. Its advantage lies in its availability without the use of an autoclave, the saving of agar and other ingredients scarcer and more expensive than rice, and its adaptability as an office method for physicians who do not wish to use the services of a mycologist.

SUMMARY

A cultural diagnostic method is described that permits the identification of ringworm fungi of the scalp, particularly species of *Microsporum*, at low cost, without agar and without special apparatus. Fourteen strains of *M. canis* and seven of *M. audouini* were isolated and identified by this method, with checking by cultures on Sabouraud medium.

370 Commonwealth Avenue

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minutes on three successive days, care being taken that the cotton plugs do not become wet except by steam. On the third day, after the bottles have been cooled to room temperature, they are ready for inoculation.

Fungi are usually isolated by inoculating the surface of a slanted medium at three to five points

The search for a medium was influenced by Conant's² extensive work on rice. This was chosen as a medium because it is available everywhere and does not undergo seasonal changes, as do potatoes. Rice was used instead of starch or flour because these materials are not so easily washed and may be unsuitable for cultures because of adulteration.



FIGURE 1. Fresh Preparations from Colonies on Gentian-Violet Rice Medium (stained with 0.5 per cent cotton blue in lactophenol).

A, *Microsporum canis* (seven-day culture); B, *M. audouini* (fourteen-day culture); C, *Trichophyton gypseum* (eight-day culture); and D, *M. gypseum* (seven-day culture).

1 cm. or more distant from one another. The gentian violet-rice medium should be inoculated only at the center of the surface, using several bottles. The material for culture is best collected under a Wood's light. Small cuts of the intradermal portion of hair stumps are used for the inoculation. The inoculated bottles are kept at room temperature.

bleaching or the addition of preservatives. Numerous samples of rice were tried, including long-grain and partially hulled (brown) rice. Only one kind of rice was encountered on which *M. audouini* did not grow unless the rice was washed. *M. canis* grew on all samples without previous washing. Slight changes in the proportion of water and rice did not

reциably alter the character of the colony or the of growth of either fungus. A high percentage water was used to keep the medium fit for inoculation for more than a month. Ordinary medicine bottles withstood the flaming of their mouths without cracking.

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In some cases hair stumps from diagnosed cases were used for culture after the patients had received topical medication. In one of these cases *M. audouini* failed to grow on either gentian-violet rice or Sabouraud medium. Fungicides were supposed to be responsible for this failure. One strain of *M. canis* from a treated patient failed to grow on Sabouraud medium but developed on gentian-violet rice.

The reported experiments show isolation of the fungi usually responsible for tinea capitis to be as successful on gentian-violet rice as on Sabouraud medium. Their features differ widely enough on the former to distinguish them from each other. These statements seem conclusive at least for *M. canis* and *M. audouini*, since fourteen and seven strains of these fungi, respectively, were isolated, numbers not exceeded in the reports of authoritative authors^{2,3} when testing a new or modified culture medium. Other species of *Microsporum* are rarities in this country. If encountered, they may be identified with the help of Conant's² taxonomic study on a polished-rice medium.

The disadvantage of the gentian-violet rice is that Sabouraud medium frequently permits a diagnosis of *M. audouini* at an earlier date. Its advantage lies in its availability without the use of an autoclave, the saving of agar and other ingredients scarcer and more expensive than rice, and its adaptability as an office method for physicians who do not wish to use the services of a mycologist.

SUMMARY

A cultural diagnostic method is described that permits the identification of ringworm fungi of the scalp, particularly species of *Microsporum*, at low cost, without agar and without special apparatus. Fourteen strains of *M. canis* and seven of *M. audouini* were isolated and identified by this method, with checking by cultures on Sabouraud medium.

370 Commonwealth Avenue

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MEDICAL PROGRESS

INDUSTRIAL HYGIENE IN 1944

IRVING R. TABERSHAW, M.D.,* AND MANFRED BOWDITCH†

BOSTON

AS in all other fields of knowledge, progress and development in industrial hygiene have been profoundly influenced by the war. This is especially true of industrial medicine, since it is second only to military medicine in its contribution to the war effort. While the laboratory continues to add its sum of knowledge, a wealth of clinical data on some of the older obscure and newer specific occupational diseases has been accumulated within the last year.

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REHABILITATION

At the outset of the war, a major problem of industry was to find a proper place for the handicapped worker — those with one eye or with an orthopedic defect, the deaf, the young and the very old, and others who under normal conditions could not compete in the labor market. Industry learned a great deal and did a magnificent job in placing these persons.² The emphasis is now changing, and the knowledge gathered during this period will have to be transposed to the absorption into industry of many veterans with physical and mental handicaps. Industry is well aware of the approaching problem, and its preoccupation with it is indicated by the number of articles published on rehabilitation, especially the plans that various industrial organizations have proposed regarding the reassimilation of its former employees and other veterans into peacetime production. All such programs visualize a medical preplacement examination in which the physician will not only evaluate the worker's disability, but will also be aware of the implications of the job for which the applicant may be fitted. Classification of disabilities and job-analysis codes have been worked out. Use of these

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The work of both groups of investigators has demonstrated that aluminum or alumina, when introduced into the animal body, will prevent silicosis provided the irritant (quartz) and the inhibitor (aluminum) ultimately localize in the same phagocytic cells. Injection of aluminum or alumina prevents further enlargement of fibrous silicotic nodules and causes the resolution of im-mature silicotic tissue. The animals injected with aluminum remain apparently healthy, and sus-ceptibility to tuberculous infection is not increased by the small amounts that are adequate to protect against silica. It seems inevitable that, with the publication of these results of many years of careful investigation, widespread clinical application will occur. It must be remembered, however, that aluminum therapy should be used only under close medical supervision and that the chief method of prevention should still be control of atmospheric dust by engineering methods.¹⁶⁻¹⁸

PNEUMOCONIOSIS

A silica hazard has appeared in the cutting and grinding of quartz crystals for use in radio trans-mission.¹⁹ The manufacture of these crystals is relatively new and undergoing constant change, but the health hazard can be effectively controlled by adequate renewal of the recirculated liquid used

for cooling the diamond-edged saw. Tripoli, which is 98 per cent quartz and produces in experimental animals the typical proliferative silicotic reaction, does not frequently cause human silicosis, although many workers are exposed. This is due to physical properties that prevent its being dispersed in the air as a dust.²⁰

Asbestosis is usually not thought of as a pre-disposing cause of tuberculosis. Two recent re-views describe cases of pulmonary tuberculosis and asbestosis^{21,22}; these findings, however, may be coincidental. Although it is true that the series is limited, the finding of an increasing incidence of pulmonary carcinoma in persons suffering with asbestosis seems too significant to be overlooked.^{23,24} The role of pulmonary allergy in industrial occupa-tions has been examined. Occupational groups most frequently affected by respiratory allergy are labora-tory workers, food handlers, jewelers, cosmeticians, pharmacists, chemists and furriers. Treatment con-sists of removal from the environment, and in some cases, desensitization.^{25,26}

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this reason.⁴⁴ Various compositions of solders containing lead have been fed to rats without producing poisoning; these compounds, nevertheless, may be toxic to human beings.^{45,46} The hazard in shipyards from handling and burning lead-painted materials has been corroborated by a number of observers. After the last war, epidemics of lead poisoning occurred when ships were dismantled or repaired. Non-lead paints and improved methods of handling lead-painted surfaces have now been devised, and a diminution in the number of cases may be expected.^{47,48}

Sodium citrate has been used in the treatment of 5 cases of lead poisoning by Letonoff and Kety,⁴⁹ who report immediate and persistent amelioration of the symptoms. There were no reactions or ill effects from the citrate, and in the majority of cases, appreciable increases in the amounts of urinary and fecal lead occurred during the therapy.

Recognition of the hazard from radium in luminescent dial painting, an operation greatly stimulated by military demands, has led to control measures designed to prevent a recurrence of the anemias and osteosarcomas that cropped up after the last war. Though no state or governmental agency has promulgated a code having the force of law, the employers in some jurisdictions, notably Massachusetts, have co-operated with the industrial-hygiene authorities to bring about admirable working conditions. In an exhaustive article, Evans⁵⁰ has reviewed the problem of radium poisoning and the methods of protection. In many dial-painting plants, as a result of his work, radon determinations of expired air are made at periodic intervals, and from this, the amount of radium stored in the body is determined.^{51,52} A tenth of a microgram is considered the maximum permissible limit, and workers who reach this level of tolerance are transferred to other work or given a vacation. The English do not use breath radon analysis, possibly owing to insufficient technical facilities, but do insist that a three-month vacation from radium work be given each year to people engaged in this occupation.⁵³ So far, no cases of radium poisoning have been reported, and a recent survey of workers exposed from one and a half to four years has revealed no evidence of incipient radium effect.

MISCELLANEOUS CONDITIONS

A vast number of chemicals are used in industry, and knowledge of their toxicity is constantly undergoing revision. Health hazards in the synthetic rubber industry have been summarized.^{54,55} Acrylonitrile, the most toxic substance employed, may enter the body by inhalation or absorption. Styrene, although a dermatitis-producing agent and an irritant of the upper respiratory tract, is not particularly toxic. Butadiene has been found to produce irritation of the upper respiratory tract, but there is no apparent danger in concentrations below the

lower explosive limit. Trinitrotoluene (TNT), since it is being manufactured in such great quantities, still occasionally produces toxemia, but urinary tests have been developed that promise to be of assistance in early determination of hazardous exposure to this substance.^{56,57}

The physiologic principles governing the action of acetone, as well as its toxicity, have been outlined in an extensive article by Haggard and others.⁵⁸ Although acetone, as used industrially, is not extremely toxic, the paper in question reviews the physiologic principles involved in the toxicology of all volatile substances. The amount of glucuronic acid excreted in the urine has been found to be a measure of absorption of certain organic compounds, such as cyclohexanone, aniline and chlorophenol, and may prove to be an early means of detecting absorption and the severity of industrial exposure to some of these compounds.^{59,60} Largent and his associates⁶¹ and others^{62, 63} have studied the effect of fluoride ingestion on experimental animals, and the toxicities of monoalkyl ethylene glycol ethers to dogs and rats have been determined.

The chlorinated hydrocarbons so extensively used as solvents and degreasers still excite great interest, and Hamilton⁶⁴ has reviewed their toxic properties in a recent article. The reports of occupational injuries attributed to these substances have been summarized by Quadland.⁶⁵ The most toxic of these substances is tetrachlorethane, with several reports of fatal poisonings recorded. It may produce acute yellow atrophy, aplastic anemia and respiratory paralysis. In cases of early poisoning, a mononucleosis may be indicative of overexposure.^{66, 67} Other reports stress the action of the chlorinated hydrocarbons as kidney poisons. This is especially true of carbon tetrachloride, which sometimes produces a clinical picture of toxic nephrosis.⁶⁸ Trichlorethylene, used therapeutically by inhalation, has produced ventricular tachycardia in several cases; this phenomenon may account for some of the mysterious deaths reported from industrial exposures to vapors of this and other chlorinated hydrocarbons.⁶⁹

Otologic injuries have recently achieved some prominence, especially in shipyards, where noise is a constant hazard. The threat of deafness to many workers employed in noise-producing operations has been outlined by McCoy⁷⁰ and others.⁷¹ Prevention is difficult, but the problem has as yet received insufficient attention. Audiometer studies of workers before, during and after employment are indicated.

Infectious disease of occupational origin is not frequent, but two types have recently been emphasized. In a study of 24 patients admitted for brucellosis to the Cook County Hospital in Chicago, only one was engaged in an occupation in which exposure might not occur; 17 were employed in packing houses, and 6 others were in contact with domestic animals.⁷² Leptospirosis has long been

The most noteworthy hazard in welding has been recognized to be the pulmonary irritation caused by fumes created by the volatilization of the welded metals. Metal-fume fever has been repeatedly described. There is no clinical evidence that any sequelae dangerous to health develop from this condition. Many workers exposed only to iron oxide have developed a pigmentation of the lung (siderosis), which apparently produces no disability or any increased susceptibility to tuberculosis or other infections, although the presence of iron oxide in the lung has been reported by at least one observer to be responsible for reactivation of tuberculous lesions and for progression of active lesions.³¹ This pigmentation of the lung has been likened to a tattoo of the skin. Many welders, however, do complain of some upper respiratory irritation characterized by a metallic taste, cough and, occasionally, blood-streaked sputum. These symptoms are related to the traumatic effect of the inhaled dense fumes of iron oxide and to the smoke of the organic materials coating the welding rods. This problem of siderosis is coming to the attention of physicians because of the increased amount of welding, and it should be borne in mind that differential diagnosis between this condition, which is entirely harmless, and acute miliary tuberculosis, fungus infections, metastatic carcinoma and silicosis is sometimes extremely difficult and must depend on the history and physical findings of the case.³²

The welding of metals other than steel or iron may produce symptoms. Recent reports, including one of 5 cases, with one death,³³ have re-emphasized the dangers from welding cadmium-plated steel. The mortality rate of metallic cadmium poisoning is estimated at 15 per cent, and the clinical picture is similar to that from exposure to the oxides of nitrogen or phosgene. Symptoms, usually delayed, may start in four to eight hours after exposure, with irritation of the throat, followed by cough and headache, and from twenty to thirty-six hours after exposure the patient may develop symptoms suggestive of pulmonary edema. Volatilization by the electric arc of other metals used as an alloy or surface coating may produce exposure to lead, manganese or chromium, but except for lead, there is little danger of occurrence of a harmful concentration.

Pulmonary disease among welders is not more frequent or severer than in the general population or in those engaged in shipbuilding occupations other than welding and having the same exposure factors.³⁴ There have been, in fact, reports of the healing of tuberculous infiltrates while the worker is still exposed.^{34,35} Technics of providing local exhaust ventilation in welding operations have occupied the engineers, and great strides have been made in this direction. The chief problem of ventilation has been in the holds of ships. Masks with supplied air have also been designed and have some merit.³⁶

DERMATITIS

Dermatitis remains the single most frequent disease directly resulting from occupational exposure. New substances introduced into industry are constantly being identified as being either primary skin irritants or sensitizers. Unpolymerized resins have become increasingly important as plastics in the manufacture of airplane and other military equipment. These vary widely and can be roughly grouped as protein glues, natural-resin glues and synthetic glues. Any of this group may be a dermatitis-producing agent, with the synthetic glues outstandingly the most frequent.³⁷

Another group of substances which has drawn attention is that of the antimildew compounds for textiles. Some of these are phenyl mercuric salts or other organic compounds that produce a sensitization dermatitis. In most cases the use of protective clothing prevents the worker from developing a skin lesion. In addition to the synthetic resins and fabric finishes for waterproofing, flameproofing and mildewproofing, antioxidants used in rubber manufacture may also be responsible for the production of a dermatitis. For instance, the monobenzyl ether of hydroquinone used in this fashion often produces a leukoderma.³⁸

The cutting oils still remain a problem. Sterilization of the oil and the introduction of antiseptics will not prevent a rash; cleanliness and minimal contact with the oil are of first importance in controlling oil folliculitis. Many of these oils have been shown to contain chlorinated compounds and hence may produce a typical chloracne. Occupational acne may also be caused by crude petroleum, coal tar and the chlorinated naphthalenes, diphenyls and benzols. Preventive measures are available, but with the chlorinated naphthalenes, and diphenyls which are used as insulation materials, these have not been entirely efficacious.³⁹⁻⁴¹

The role of patch tests in occupational dermatitis has been reviewed by Downing⁴² and Schwartz.⁴³ The most comprehensive article is by Schwartz, who points out that patch testing with industrial materials demands careful attention and precise knowledge, and even then a whole gamut of errors is possible. A negative result does not rule out the tested substance as a causative agent, since it is impossible to duplicate actual working conditions by this test. Criteria for the diagnosis of occupational dermatoses have been established, however, and the methods of control that have been devised are adequate if applied properly and in time.

LEAD AND RADIUM

Experimental studies in the toxicity of lead have demonstrated that a number of lead-containing substances finding increasing industrial use are soluble in tissue fluids. Lead borosilicates used for ceramics and for glass bushings are potentially toxic

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EDITH E. PARRIS, *Assistant Editor*

CASE 30471

PRESENTATION OF CASE

A forty-one-year-old woman, a millworker, was admitted to the hospital with dyspnea.

The patient was in good health until four months prior to admission, when she developed a cold, followed in a few days by a cough productive of small amounts of whitish sputum. There was no fever or malaise. The cough persisted, but she was able to work. About a month later she suddenly developed sharp inspiratory pain along the right costal border anteriorly and posteriorly. At the same time she noted that she was moderately dyspneic at rest. She continued to work, and her symptoms disappeared after a week. One month later, about six weeks prior to entry, dyspnea recurred and became so severe as to prevent all normal activity. At that time she was examined at a local hospital, a roentgenogram revealing a massive pneumothorax on the right, with basal effusion. The right lung was completely collapsed, and the mediastinum was displaced markedly to the left. From then until admission, she remained dyspneic and was limited to bed and chair activity. Eating aggravated the cough, and on one occasion she claimed to have coughed up about a cupful of "yellowish pus." She was unable to breathe when lying on her left side. She had lost 27 pounds during her illness.

Except for a hysterectomy eleven years previously following attempts at self-abortion, her past history was negative.

Physical examination revealed a sturdy, moderately obese woman propped up in bed, in moderate respiratory distress. The trachea was moderately deviated to the left. The chest showed diminished expansion on the right. The percussion note was about equally resonant on both sides. Tactile fremitus and breath sounds were practically absent on the right, and a few musical rales were audible in the right axilla and over the right base. The apical impulse was felt in the fifth interspace in the anterior axillary line, but there were no auscultatory abnormalities.

*On leave of absence

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 90 diastolic.

Examination of the blood revealed 70 per cent hemoglobin and a white-cell count of 12,200. The urine gave a + test for albumin, and the sediment contained 5 to 10 white cells per high-power field. Sputum culture on two occasions revealed beta-hemolytic streptococci.

Roentgenograms of the chest showed the right lung to be composed almost entirely of large cysts (Fig. 1). The upper lobe appeared destroyed, and numerous smaller cystic structures were present in the middle and lower lobes. The right main bronchus was visualized for a distance of 2 cm. but was not well seen beyond that point; no intrinsic lesion could be demonstrated, however. The heart and mediastinum were displaced to the left, somewhat compressing the left lung. Laminograms of the chest revealed a suggestive but indefinite shadow in the right main bronchus.

On the second hospital day the right chest was decompressed, 750 cc. of air being removed. The patient felt much relieved, but the chest signs remained unchanged. Two attempts at bronchoscopy were unsuccessful.

On the twenty-first hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RALPH ADAMS†: The initial cough productive of small amounts of whitish sputum, without fever or malaise, indicated an attack of bronchitis. Sharp inspiratory pain a month later was a sign of pleural involvement. Its location along the anterior and posterior chest wall is typical of the referred pain of pleural irritation, it being expressed along the somatic fibers of the posterior and anterior penetrating branches of the intercostal nerves. Dyspnea even at rest implied pulmonary insufficiency, presumably from pneumothorax. The symptoms disappeared as the intrapleural air was absorbed. A pulmonary leak recurred one month later, and dyspnea was severe because of tension pneumothorax and pleural effusion. Roentgenologic examination at a local hospital furnished confirmation. The markedly displaced mediastinum and completely collapsed right lung provided an explanation of the dyspnea.

The patient remained dyspneic even in bed because of limitation of the respiratory reserve by the abnormal intrathoracic pressures. Most patients with a cough find it aggravated by eating. The coughing up of about a cupful of "yellowish pus" probably represented the raising of fluid spilled out of a previously blocked cyst. Her inability to

†Surgeon, Lahey Clinic, Boston

known to be occupational, in that miners and others frequently develop the condition as a result of contact with ground water infected with the urine of diseased rats. Fourteen such cases were recently reported in an Alabama mine,⁷⁸ and there has been an outbreak of the same disease in a New England fishery. Although carrying a grave prognosis, two of the former cases were cured with penicillin.

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can be obtained from the Bucky film, namely, suggestion of a lesion in the right main bronchus. The left lung field appears to be normal.

DR. ADAMS: Will you put up the left anterior oblique film?

DR. ROBBINS: In this film the right main bronchus can be seen to this point.

DR. ADAMS: Your interpretation differs from the record.

DR. ROBBINS: It should not, because I gave most of the interpretation.

DR. ADAMS: The record states, "No intrinsic lesion could be demonstrated." Is that still your impression?

DR. ROBBINS: I cannot be positive that there is a lesion there, but I am suspicious because of the Bucky film and because of the fact that one can follow the right main bronchus to a point where it stops abruptly.

DR. ADAMS: Experiences at these exercises heretofore have taught me that the more apparent the diagnosis, the more carefully one should seek the unemphasized morsel of evidence (the "red herring" or, more explicitly, the "hidden slug"). I have therefore looked diligently for clues to some collateral morbid process in this case. The negative evidence is important only in the process of exclusion. The patient did not have hemoptysis, as practically always occurs at some time in some degree with bronchiogenic tumor, whether benign or malignant. By x-ray examination the primary bronchi were found open and clear. One cannot, then, properly retain bronchial adenoma or pulmonary carcinoma for causative consideration. She did not have a chronic cough productive of purulent or foul sputum, and since this is a constant concomitant of bronchopulmonary suppuration, that diagnosis also is untenable. The sputum apparently contained no tubercle bacilli; furthermore, there was no wheeze, and bronchial stricture is the only means by which tuberculosis could have led to the recorded cystic destruction. Tuberculosis is hardly worthy of inclusion in the differential discussion.

I confess, however, that I am still troubled by one point. The left anterior oblique film, taken to demonstrate the bronchi of the right lung in profile view, shows a niche in the lateral wall of the right primary bronchus, beginning 5 mm. below the carina, and itself 7 mm. in length (Fig. 1). Immediately above the niche is a curved cylinder of radiolucence 2 mm. in width and 6 mm. in length, lying in the position that a right-upper-lobe bronchus normally occupies. But it is too small for the right-upper-lobe bronchus, and too large for an artefact. Unfortunately, the laminographer did not record a section film at the proper depth to show the right bronchial tree, and bronchoscopy was not possible. One is again reminded of the frequently essential nature of bronchoscopy in establishing an accurate

pulmonary diagnosis. Notice that the margin of the niche in respect to the primary bronchus is concave, as would occur with fibrosis and scar contraction, rather than convex, as would occur with a propagating tumor. The remnant of the upper-lobe bronchus is so narrow that edema, as from bronchitis, could easily prevent egress of air, and be followed by rupture of the cyst and spontaneous pneumothorax, which would initiate the clinical and physiologic history of this case.

After devoting so much time to the clinical and physiologic features, I shall briefly discuss the anatomic and pathologic features of the disease. Many forms of pulmonary cysts no doubt are acquired, as by parenchymal dilatation from hemorrhagic effusion or distention from infected secretions distal to bronchial obstruction of an inflammatory nature. Cystic bronchiectasis, statistically the most fatal form, is the prime example of this type. Emphysematous blebs lying subpleurally, with a background of asthma or pulmonary fibrosis, comprise a second acquired type. Closely similar are the huge solitary cysts that occur as late complications following the inhalation of a noxious gas. Phosgene poisoning in World War I contributed several cases to this group, one of which I treated surgically only eighteen months ago, twenty-five years after the initial injury. The majority of cysts, however, are believed to be congenital in origin. A lining membrane of ciliated epithelium is generally present, and anthracosis in the residual lung parenchyma is infrequently found, intimating lifelong failure to aerate that portion of lung. The frequency of associated bronchial and vascular abnormalities is high.

Some cysts contain viscid albuminous fluid consisting chiefly of epithelial debris, as well as air; they may empty spontaneously and then refill with air under tension. The patient coughed up a cupful of such material and called it "pus." The postnatal behavior of the congenital type is influenced by the amount and manner of bronchial communication and above all by the time and virulence of complicating infection. The disease is likely to be clinically silent until a check-valve mechanism is established in a communicating bronchus. In this patient it was silent for forty-one years.

I assume that the operation was a pneumonectomy. On the basis of a small experience with this disease, I am willing to predict that the operative and pathological examinations of the specimen showed a pulmonary artery of much smaller diameter and greater thickness of wall than normal, fibrosis and scarring of the right-upper-lobe bronchus with production of a check-valve mechanism, lower-lobe bronchial dilatation of the cystic rather than the truly bronchiectatic type, parenchymal destruction by cysts lined with either ciliated or flattened

breathe when lying on the left side was caused by mediastinal pressure on the already somewhat compressed and only functioning lung. It illustrates the fact that almost every patient with a critical chest condition can breathe better with the afflicted hemithorax lower than the opposite one. She had lost 27 pounds from interference with normal food intake by coughing and from the increased work of dyspneic breathing. The past history seems irrelevant.

Physical examination revealed the findings to be expected in a patient suffering from tension pneumo-

in this hospital, one may properly ask why two attempts at bronchoscopy were unsuccessful. The usual reasons, occasionally encountered, are cervical arthritis, a totally unco-operative patient and a receded lower jaw (best described as a "Burn Gump chin").

The diagnosis of cystic disease of the lung is obvious. The history is classic, a previously healthy patient in early middle age suddenly developing serious symptoms following a minor respiratory infection. The physical signs are those to be anticipated following rupture of one of the cysts into

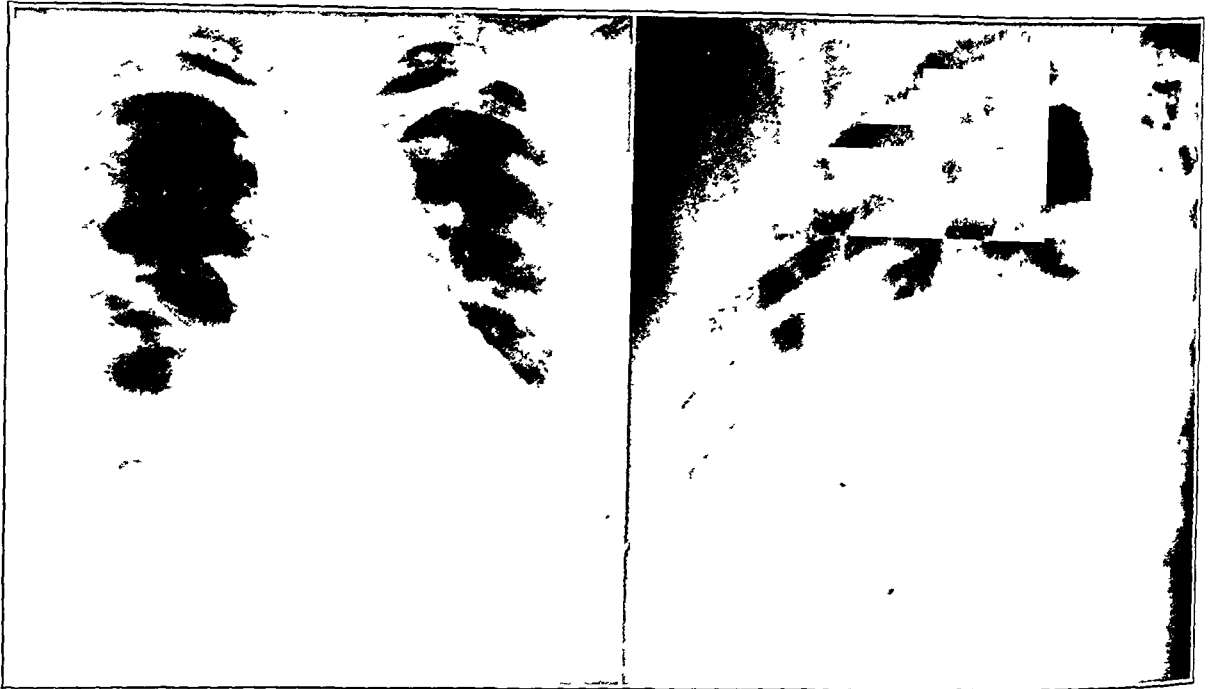


FIGURE 1 Anteroposterior and Left Anterior Oblique Roentgenograms of Chest.

thorax with mediastinal displacement into the opposite hemithorax.

The data of the clinical chart indicate that she was in cardiac equilibrium at bed-rest conditions and that she was free of major infection.

Laboratory examinations disclosed a mild secondary anemia and leukocytosis, which could be attributed to the diminished food intake, the chronic respiratory illness and the bronchitis. The urinary findings have no discernible significance. Proof of bronchial infection was found in the sputum culture, which on two occasions revealed beta-hemolytic streptococci.

The roentgenograms were typical of so-called "cystic disease of the lung" and failed to establish evidence of any primary bronchial obstruction.

Decompression of the right chest gave relief by removing pressure on the left lung rather than by restoring function in the right lung. With the excellent endoscopy service known to be available

the pleural cavity secondary to a valve-type obstruction of its small bronchial communication by streptococcal bronchitis and associated edema. The case presentation gives a detailed description of cystic disease in the x-ray report, with a directness of terminology that is not designed to confuse one in doubt of the diagnosis.

DR. LAURENCE L. ROBBINS: The heart and mediastinum appear to be displaced a little to the left indicating that the large cystic structures on the right are under tension. In the lateral view we simply obtain more information about the number and size of these cystic cavities that appear to involve the entire right side of the chest. The Buckley film and grid film clearly demonstrate the trachea and right main bronchus. The trachea appears to bifurcate normally, and the right main bronchus can be seen for a short distance and then stops rather abruptly. The laminogram was not entirely satisfactory and does not give any more information

epithelium: the walls were composed predominantly of smooth muscle with scattered foci of mucous glands and a rare group of cartilage cells. This lesion was therefore a true bronchiogenic cyst.

DR. ADAMS: What about the right-upper-lobe bronchus?

DR. CASTLEMAN: I should think that it was compressed by this cystic mass in such a way as to produce the narrowing observed in the film; we have not investigated that point, however. The lung parenchyma, except for being atelectatic, was normal.

DR. ADAMS: Do you think that it was a form of congenital cystic disease?

DR. CASTLEMAN: Yes. The usual theory of the origin of a bronchiogenic cyst is that it is the result of the pinching off of a lung bud during embryonic life. It increases in size so long as there is a communication with a bronchus. This one is the largest that we have ever seen. They are usually located in the upper mediastinum close to the bifurcation of the trachea.

CASE 30472

PRESENTATION OF CASE

A fifty-year-old man, a former credit manager, entered the hospital because of pain in the back.

The patient had been in good health until two months before admission, when he noticed gradual onset of pain low in the back. The pain gradually increased in intensity, was more or less steady and ranged from "dull to very severe." It was aggravated by coughing and sneezing and was worse when he was flat in bed, so that after a night in bed, he found it difficult to move at all. He obtained some relief by standing or walking and by taking aspirin and Empirin. Every two or three days he also noted pain in the right lower quadrant of the abdomen, which was sharp and crampy in character. With the onset of the pain in the back, the patient also developed severe constipation. Once or twice he noticed bright-red blood in the stools, which he attributed to hemorrhoids. There was considerable straining at stool. When severely constipated the abdomen became distended, but he had no nausea or vomiting. The distention and constipation were relieved by cathartics. His appetite, which had always been good, remained unchanged. He had lost 12 pounds in eight months. About four days before entry he developed edema of both ankles, but there was no dyspnea, chest pain, cough or hemoptysis.

One year before entry, repair of a recurrent inguinal hernia and an appendectomy were performed.

Physical examination showed a well-developed, well-nourished man in moderate distress. The left

border of cardiac dullness was 10 cm. to the left of the midline. An apical blowing systolic murmur was heard. The lungs were clear. There was some tenderness to deep palpation in the right lower quadrant. Palpation anywhere in the abdomen caused pain in the back. Along the crest of the right ilium posteriorly there was tenderness to palpation. Rectal examination was negative except for external hemorrhoids. There was pitting edema of the ankles and feet.

The blood pressure was 145 systolic, 90 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

Examination of the blood showed a red-cell count of 4,250,000, with 12.6 gm. of hemoglobin. The white-cell count was 6800, with 73 per cent neutrophils. The urine was normal. A blood Hinton test was negative. The serum protein was 7.2 gm. per 100 cc. The nonprotein nitrogen was within normal range.

Anteroposterior and lateral films of the lumbar and dorsal spine and plain films of the abdomen and chest were normal. A barium enema was not entirely satisfactory, but appeared to be essentially negative.

On the second hospital day the patient had considerable pain low in the back, and 16 mg. ($\frac{1}{4}$ gr.) of morphine was given. The pain gradually subsided in the next four or five days. During that time he apparently had difficulty with urination. On the sixth hospital day he experienced numbness over the anterior aspects of both thighs and there was diminished sensation to pinprick. The ankle jerks and knee jerks were brisk and equal, and the plantar reflexes were normal. There was no marked atrophy or weakness, but the pain was so great that accurate testing was impossible. Sudden muscular contraction produced acute sharp pain. The upright position seemed to produce steady severe pain low in the back. An intravenous pyelogram showed prompt excretion of the dye by both kidneys, but the pelves and calyces could not be visualized because the patient experienced a severe reaction, the nature of which is not described in the record. On the seventh hospital day an exploratory laparotomy revealed no abnormal findings. Postoperatively the edema disappeared completely.

On the tenth hospital day lumbar puncture between the first and second lumbar vertebrae gave clear yellow fluid that clotted on standing. The initial pressure was 130 mm. of water; jugular compression caused a prompt rise of pressure to 220 mm. and a subsequent fall to 200 mm. This procedure produced considerable pain low in the back and in the abdomen. Ten cubic centimeters of fluid was removed giving a final pressure of 80 mm. The total cell count was 2 per cubic millimeter. The ammonium sulfate ring test was + + + +, and the total protein 1140 mg. per 100 cc.

epithelium and relative absence of carbon pigment.

In conclusion, my diagnosis is congenital cystic disease of the right lung.

DR. BENJAMIN CASTLEMAN: Dr. Drake, will you describe the operation?

DR. EMERSON H. DRAKE: Our preoperative conclusions were similar to those of Dr. Adams. We thought that the lesion in the oblique view might represent a bronchial lesion of some sort and that we might run into a right lung that was completely destroyed because of cystic disease. The patient had been rather unco-operative. She was a thick-

CLINICAL DIAGNOSIS

Congenital cystic disease of lung.

DR. ADAMS'S DIAGNOSIS

Congenital cystic disease of lung.

ANATOMICAL DIAGNOSIS

Bronchiogenic cyst, extrapulmonary.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The specimen we received was a completely collapsed right lung to which was

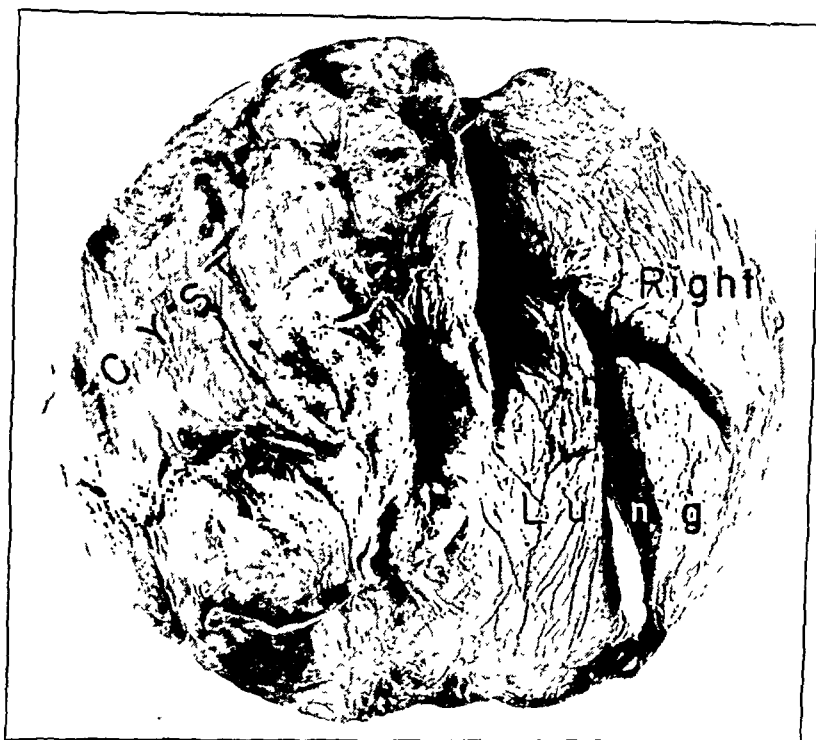


FIGURE 2. Photograph of Cystic Mass Attached to the Right Lung.

necked, husky individual and it was impossible to pass the bronchoscope on two occasions.

On opening the chest cavity, the cystic mass obviously contained air. It was thick-walled and dense, and the two pleural layers were adherent. The cystic mass was freed with difficulty from the parietal pleura. An area of collapsed lung, which appeared to be middle lobe, was visualized, but the size of the cyst made it practically impossible to expose the hilum clearly. At one point a small tear was made in the cyst wall, following which a small amount of mucoid material exuded. We were unable to separate any normal lung tissue from the cystic mass, and the whole lung was removed en masse.

The postoperative course was uneventful. She has been seen during the past month and is asymptomatic.

attached on its lateral and posterior portions a huge cystic structure that compressed and rotated the lung so that it lay posteriorly and medially in the chest and thus could not be identified during the operation. The mass measured 25 by 15 by 11 cm. and was attached to the surface of the lung in two places — one at the upper lobe and the other over a large area of the lower lobe (Fig. 2). The attachments over the lower lobe were dense and were exceedingly difficult to separate without tearing the lung. No bronchial communication could be demonstrated.

Section of the mass showed that it was composed of one large cavity, comprising the upper half, and a number of small cavities, occupying the lower half. The walls of the spaces were made up of dense fibrous tissue and were heavily trabeculated. Microscopically the cysts were lined by respiratory

short length, in other words, not a lesion that tended upward for any distance. The symptoms had been going on for a relatively short period of time. Although they progressed rapidly I do not believe that that necessarily implies the nature of the lesion. We must consider all the lesions usually seen at this level. Ependymoma is unlikely, because the site was above the lower end of the conus and an ependymoma is rarely seen there; when it does occur, it is intramedullary rather than extramedullary. In view of the relatively rapid progress of the disability and the absence of a history of injury the leading possibilities are meningioma and neurofibroma, in that order, with a ruptured disk a poor third.

DR. AUGUSTUS S. ROSE: This case is a good example of how "red herrings" can interfere with judgment. I saw the patient prior to the abdominal exploration, along with Dr. Richard Miller and Dr. Wyman Richardson. Dr. Lewis has properly evaluated the edema of the legs, which we failed to do. The man had predominantly abdominal symptoms, we thought, with a palpable liver and tenderness of the abdomen, together with edema that was rather more marked than is intimated by the abstract. I thought that there was a retroperitoneal mass, with obstruction of the vena cava. The patient was difficult to examine that an accurate diagnosis was impossible. The pain was excruciating, and although the comment is made that he received 10 mg. of morphine at one time, he actually received as much as 32 mg. two or three times a day. The pain was literally everywhere below his chest, and whereas it was severer in the back, it was widely distributed. I make these statements not only to defend our course but also to emphasize the unusual features of the case. I made the great error of not doing a lumbar puncture, in spite of the negative neurologic examination. We were swayed by abdominal exploration was performed. A lumbar puncture was done after the negative abdominal exploration, and clear-cut evidence of a

dynamic and chemical block was found, so that a diagnosis was possible.

DR. JAMES B. AYER: Why did the edema disappear after the lumbar puncture?

DR. ROSE: We believed that the edema was postural. The patient could not lie down in comfort, having been forced to sit in a semiupright position or to stand for two months. With hospitalization and abdominal surgery he was forced to lie down, which gave the edema an opportunity to subside.

In retrospect it may be of interest that the onset of the man's pain, which we did not determine until after the operation, came on immediately after he tripped in coming out of a streetcar. He missed the curbstone and came down hard on the extended leg. Pain came on instantaneously and was present intermittently until the time of the operation.

DR. LEWIS: The omission of this history of injury may be significant; it might cause a change in the diagnosis.

DR. ROSE: He did not fall. He simply missed the curbstone as he stepped from the car.

CLINICAL DIAGNOSIS

Spinal tumor.

DR. LEWIS'S DIAGNOSIS

Meningioma?

Neurofibroma?

ANATOMICAL DIAGNOSIS

Neurofibroma.

PATHOLOGICAL DISCUSSION

DR. KUBIK: Dr. W. Jason Mixer performed the operation. On removing the laminae of the eleventh and twelfth thoracic vertebrae he came down on a tumor lying beneath the dura and arachnoid membrane. The tumor, a neurofibroma, was 3 cm. long and 1.5 cm. in diameter.

The patient made a good recovery.

After lumbar puncture there was a questionable level of sensory disturbance in the right groin. On the sixteenth hospital day, lipiodol injected at the fourth interspace was arrested between the twelfth dorsal and first lumbar vertebrae (Fig. 1). On the eighteenth hospital day a laminectomy was performed

DIFFERENTIAL DIAGNOSIS

DR. SAMUEL LOWIS: There are several peculiar things in this case. Some of the difficulties even-



FIGURE 1

tually disappeared, but some of them resulted in an operation that apparently yielded no information concerning the basic problem.

We are told that the patient was in good health until two months before admission, but he began to lose weight eight months before admission despite a normal appetite. The pain was of a type frequently seen with an intraspinal lesion in the lumbar area; that is, it was dull to severe, aggravated by coughing and sneezing, and worse when lying flat in bed. It apparently increased markedly during the time in the hospital, although that is not specifically stated; in spite of this pain, neurologic examination was negative. We are told that the patient had marked abdominal symptoms because of which pyelograms and a barium enema were done, with essentially negative results. In spite of this and without any other given information an exploratory laparotomy was performed, with no

abnormal findings. Is a preoperative diagnosis available?

DR. CHARLES S. KUBIK: It was retroperitoneal lymphoma.

DR. LOWIS: One not infrequently sees abdominal symptoms but quite rarely abdominal signs with lumbar, intraspinal, expanding lesions once they have reached the point of compressing the structures within the spinal canal. We are told that pressure on the abdomen caused pain in the back which is a reasonable finding in terms of a lesion that filled the spinal canal: pressure on the abdomen causes an increase in the intraspinal pressure by back pressure on the lumbar veins, and may cause a shift in the position of the tumor in relation to the nerve roots about it or an increase in the pressure of the mass on the nerve roots. We are told that the patient had urinary difficulty while he was in the hospital. This, too, may be considered to have been a sign of an intraspinal lesion, although one cannot be definite because it disappeared before treatment. We are told particularly, and this seems to me to be of interest, that the pain was rather marked, steady and crampy, and worse when he lay flat on his back, and therefore worse in the morning. This is the kind of pain that one sees not uncommonly with intraspinal lesions that have caused a considerable degree of pressure on nerve roots for a long time. Usually when this has happened there are positive neurologic findings, but their absence is not against an intraspinal lesion. We can overlook the edema: not because it is of no importance but because I can see no way to tie it in with the clinical findings in the history.

May we see the x-ray films? There is no question that there was total block. The fluid had a high protein content and clotted; and I think that we can assume there was no recent inflammation because of the low cell count. The dynamics were consistent with block, though we are told nothing about abdominal compression.

DR. LAURENCE L. ROBBINS: In the plain films of the spine I can see nothing of significance, but the lipiodol examination apparently gives the answer. When this was injected into the subarachnoid space through a needle in the third lumbar interspinous space, it was arrested opposite the twelfth thoracic vertebra.

DR. LOWIS: The distance between the pedicles was measured, I assume, and was normal.

DR. ROBBINS: Yes, and there is no apparent erosion of the pedicles.

DR. LOWIS: There is no history of injury; this is of some significance because one rarely sees a ruptured disk at that level and, when one does, there is generally a history of severe trauma to the back, usually direct. It seems to me that with a lesion in that location, which is about at the conus of the cord, and in the absence of signs referable to the cord itself, the lesion must have been

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e unvaccinated.^{3,4} It is also generally agreed at the attacks that occur in vaccinated children e less severe than those in the unvaccinated.^{2,4} In Massachusetts from 1924 to 1943, 58 per cent all the deaths from this disease occurred in the st year of life, and 84 per cent in the first two ars. The protection of infants from exposure to whooping cough continues to be a vitally important ctor in the control of this disease; the vaccine, wever, is usually not effective in the first six onths of life. Furthermore, reactions are likely be severest at this early age.⁵ The first injection ould be given in the seventh month. The best munity is achieved by giving three subcutaneous jections one month apart. The height of im- nity is reached after three or four months. A ngle dose one or two years later to "boost" the munity is a sound practice and should be en- uraged. Since the incubation period of whooping ough is only about ten days, one should not expect y benefit from vaccine administered to a child ter exposure to the disease, much less after the set of symptoms.

Pertussis vaccine may be combined with diphtheria xoid without producing untoward results follow- g injection, but preparations also containing tanus toxoid produce such severe reactions² at, at the moment, they are unsatisfactory.

Cohen and Scadron⁶ injected pregnant women ith *H. pertussis* vaccine with the result that a high iter of immune bodies developed in the mother nd was transmitted to the baby. As pointed out y Lapin, "such antibacterial passive immunity is notoriously short-lived . . . and no clinical evi- ence of protection against exposure has been forth- oming." Therefore, how much actual protection rom such placental transmissions of antibodies ill come from this method remains to be seen.

Hyperimmune serum supplies a certain degree f temporary passive immunity, and because of this s often effective as a prophylactic measure after xposure in the first months of life. Such protection, owever, does not extend beyond fourteen days. This serum is also of value in the early stages of the isease itself. Indeed, in many institutions it has become routine procedure on admission in all cases

of pertussis in which the children are under two years of age.

Besides hyperimmune serum, advances in the treatment of whooping cough include the use of oxygen in cases in which repeated convulsions result from the anoxemia brought about by severe paroxysms.⁷ Needless to say, oxygen will not control the repeated convulsions that are due to cerebral hemorrhage.

In a disease with such wide variations in severity, it is difficult to determine the value of the various agents that have been said to be of benefit. This is proved by the figures compiled by Stimson⁸ at the Willard Parker Hospital, which showed that, with no particular change in therapy during nine years, the mortality from pertussis varied from 8.8 per cent in 1931 to 2.1 per cent in 1939. In Mas- sachusetts, the fatality rate fell rather steadily from 2.4 per cent in 1927 to 0.4 per cent in 1942. It is to be hoped that with intelligent and wide use of a reliable vaccine even better control of whooping cough will be achieved.

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DUDLEY — Oscar A. Dudley, M.D., of Shrewsbury, died October 28. He was in his sixty-first year.

Dr. Dudley received his degree from Tufts College Medical School in 1907. He had been the health officer of the Massachusetts Department of Public Health for the Worcester district for twenty-five years. He was decorated with the Croix de Guerre by the French government for heroism in World War I. Dr. Dudley held a commission in the Massachusetts National Guard of the United States Army for twenty-eight years, retiring in July, 1939, with the rank of colonel. He was a member of the American Medical Association and the Massachusetts Public Health Association.

His widow and two nephews survive.

MORSE — Frank L. Morse, M.D., of Somerville, died November 5. He was in his seventy-fourth year.

Dr. Morse received his degree from Harvard Medical School in 1894. He had been medical inspector in Somerville

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THANKSGIVING

DESPITE the prospect, at this date, of another winter of war in Europe with the misery and the loss of life that it entails, and of still unnumbered months to come of the struggle in the Pacific, there is yet every reason why we should proclaim and celebrate our accustomed day of thanksgiving.

We can be thankful, despite the grimness of the present and of the immediate future, that we can clearly see the eventual triumph over our enemies. We can be thankful that years of soft living have made no permanent inroads on our national vitality, that our leaders and our youth have measured up to the task that has been set before them. We can be thankful, in a year of stress, when many privileges have been curtailed and many among us have yielded

to the temptation of exercising undue authority, that we have held a national election and have chosen our leaders and our representatives according to the laws expressed in our constitution. We can be thankful that we have retained this freedom of speech and of action when freedoms in other parts of the world have been destroyed or are being restricted and limited by the hard hand of domineering authority. We can be thankful that we have been able to feed ourselves and others, well, if not lavishly. We can be thankful that the medical and surgical care given to our men in service is the best in the world and that those physicians who are left have strength to serve their communities ably and with faith. We can, in short, be thankful that the principle of liberty still prevails and will prevail.

And what can the nation do to show its gratitude for these basic blessings that so set it apart from the rest of the world? It can continue its part as a loyal, hard-working rear echelon to its armies in battle and to its fleets that have at last secured the freedom of the seas. It can work without complaining, endure without breaking, contribute without holding back and, through the Red Cross, give its own blood in safety to make up in part for the blood that has been shed for it in mortal danger.

THE CONTROL OF WHOOPING COUGH

RELIABLE pertussis vaccine has been available in the United States since 1931.¹ Such vaccine consists of whole, killed, Phase I strains of *Haemophilus pertussis*. Extracts of the bacilli have not proved to be effective immunizing agents. In the near future the Massachusetts Department of Public Health expects to supply a vaccine. With this in view, it seems appropriate to clarify what can be expected of this vaccine in the control of whooping cough.

The value of whooping-cough vaccine in the prevention of this disease in nonexposed children is much less than that of vaccination against smallpox. Lapin² has given an excellent summary of the studies on immunization in his recent book. In the presence of definite household exposure one can expect 30 to 36 per cent of the vaccinated children to become infected, compared with 92 per cent of

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JUSTICE AND THE FUTURE OF MEDICINE*

WENDELL BERGET†

WASHINGTON, D. C.

I confess that I stand somewhat in awe of my subject. Justice, medicine, the future, are mysteries about which man can know but little. My profession is the law, which aspires to, even though it does not always attain, justice; about it I am humble enough to be very humble in my knowledge. My profession is medicine; about it you are far more conscious than I as to the vistas that have not been reached and the depths that have not been probed. And the future hangs on far too many threads that are alien to your ship and to mine for either of us to boast that he can chart its course. As a layman in respect to medicine, you are wiser than I in regard to law. But the fact that we differ in training and in experience is an asset. It enables us to speak our separate minds, to compare our viewpoints, to sharpen our differences, to move toward a common understanding.

The law is no mean challenge to the human understanding. Yet my admiration goes out to physicians for the greater mystery that they have set themselves to unravel. For a casual nature has spent countless aeons in putting together that bewildering organism we call man, and a process of discovery has used up millenniums in finding out enough about how the trick was done to help man struggle with his ills and aches toward health. It has taken courage, intelligence, a myriad of guinea pigs and sacrifice of a thousand ancient truths to come far as you have on a trail that still leads into the unknown.

For the man of which medicine is mindful is a curious and wonderful thing. A long course of geologic, geologic and biologic events has made of the permutation of things that anatomically is. Nature, a slow and uncertain workman, took a fraction of eternity in which to make tries, beat retreats, blunder along its creative way. It achieved

in man a result that, if nothing to brag about, is at least passable. The chances against his being here at all are as legion to one; the chance of his being exactly what he is — well, write your own odds.

But the biologic process alone did not create man, for every human being has a distinct culture stamped all over him. At work and at play he is beaten on by a continuous stream of stimuli from the human life pulsing about him. In taking care of himself, finding a way of life, begetting posterity, going on a tear, his pursuit of happiness is pent in by the prevailing culture. Man cannot exist apart from the ways and the beliefs of the folk. We are all of us products alike of the earth and of culture, and adjustment to nature and society, always in process yet never completed, is the condition of our life.

Thus the patient—a curious and stubborn bundle of organs and ailments and resistances—presents a series of enigmas that challenge the skills of the doctor. The man on whom all medicine converges is ancient in contrast to the youthful art that serves him. He was established in his anatomic estate and fitted out with his physiologic heritage long before the “physician” was so much as a word. He bears in structure and function, in organ and senses, the impress of all that the life back of him has met in the ages it has passed through. And, to complicate the problem, man is infinitely variable. The mixture of genes, chromosomes and unit characters into fresh combinations in every individual makes each of us a new experiment. In a word, the doctor's challenge is not a standardized man. My hat is off to the man of medicine for the sheer audacity of the task he has undertaken.

From the medicine man of old to the modern clinic is a long way. Again and again mystery after mystery has been probed; again and again the utterly impossible has won acceptance against ancient truth; again and again the reach of medicine has been enlarged. The doctor's craft, with triumph after triumph to its credit, is still on its way, yet it is set within a larger problem of human well-being

*Presented at the fourteenth annual meeting of the American Urological Association, St. Louis, June 21, 1944.
†This address originally appeared in the November, 1944, issue of the *Journal of Urology*, and is reprinted, with minor changes, by permission of the editor, Dr. Hugh H. Young.
†Assistant Attorney General of the United States

from 1901 until his retirement in 1942. He was an intern at Boston City Hospital, where he became assistant resident physician. At the start of World War I, Dr. Morse enlisted and subsequently was assigned to the Surgeon General's Office in Washington. He went overseas as sanitary inspector of the 89th Division and served with the Army of Occupation. On his return to this country, he was commissioned in the Officers' Reserve Corps and held the rank of colonel until retirement in 1935.

His widow and two sisters survive.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

LANDMAN — Elbert A. Landman, M.D., of Plaistow, died October 18. He was in his seventy-seventh year.

Dr. Landman received his degree from Dartmouth Medical School, Hanover, in 1899.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Health Education on the Industrial Front: The 1942 Health Education Conference of the New York Academy of Medicine. 8°, cloth, 63 pp. New York: Columbia University Press, 1943. \$1.25.

This small volume is made up of the papers read before the Health Education Conference of the New York Academy of Medicine in 1942. They are of timely interest because of the vital interrelations of industry, labor, medicine and government. The following topics are discussed by various authorities: the wartime industrialization of the community and its health implications; food and nutrition in the home and in the work place; disease and handicap detection and control in industry; mental problems and morale in industry; and educational methods and control of accidents in industry.

The Four Hundredth Anniversary Celebration of the De Humani Corporis Fabrica of Andreas Vesalius. Publication No. 7, Historical Library, Yale Medical Library. 4°, cloth, 67 pp., illustrated, with frontispiece. New Haven, Connecticut: Historical Library, Yale University School of Medicine, 1943. \$2.50.

This small bound pamphlet is comprised of the various papers read at the celebration of the four-hundredth anniversary of the printing of the famous anatomy of Vesalius. The papers are reprinted from the December, 1943 issue of the *Yale Journal of Biology and Medicine*, and are here brought together in a volume suitable for ready reference.

Army Surgeon. By Genevieve Fox. With illustrations by Forrest Orr. 12°, cloth, 244 pp., illustrated. Boston: Little, Brown and Company, 1944. \$2.00.

In this book for children Miss Fox relates the story of Alexis St. Martin and Dr. William Beaumont. The story begins with the early life of Beaumont and continues through the period when he was studying the action of the gastric juices on his famous patient, Alexis St. Martin, and ends with the story of the travels of Dr. Beaumont and his patient to Washington and other Eastern cities, where he lectured and exhibited his patient. The book is well written in an easy style and should prove interesting to children in the teen age.

Summary of State Legislation Requiring Premarital and Prenatal Examinations for Venereal Diseases, by Aneta E. Bowden, M.A., Ph.D., and George Gould, M.A., LL.B., assistant director, Division of Legal and Protective Services, American Social Hygiene Association. Second edition, revised by George Gould. 8°, paper, 30 pp. New York City: American

Social Hygiene Association, in co-operation with United States Public Health Service, 1944.

Two years having elapsed since the first edition of this pamphlet was published, it is now found necessary to issue a new edition. During this relatively short period four additional states passed premarital examination laws, four states enacted into law bills dealing with prenatal examination and many other states amended existing premarital legislation. Thirty states have laws protecting marriage by requiring examination of both bride and groom by a physician to include a blood test for syphilis, and a like number of states protect babies by requiring the physician to examine the prospective mother for syphilis as early as possible during pregnancy. This summary provides up-to-date information on all state legislation and can serve as a practical guide to all persons concerned. The California premarital law is suggested as a basis in drafting similar laws. Premarital and prenatal charts show the operation of the respective laws in every state. A new table has been added, giving the legal waiting period in relation to marriage licenses. Each state reference has been revised in accordance with information received and approved by the individual state officers. This small pamphlet is a valuable reference text for all libraries and interested persons.

The Medical Clinics of North America. Chronic Diseases (March, 1944). 8°, cloth, 233 pp., illustrated. Philadelphia: W. B. Saunders Company, 1944. \$3.00.

NOTICES

ANNOUNCEMENT

Following discharge from military service Dr. Newman Cohen has resumed the practice of neuropsychiatry at 475 Commonwealth Avenue, Boston, Massachusetts.

NEW ENGLAND PEDIATRIC SOCIETY

There will be a meeting of the New England Pediatric Society on Wednesday, November 29. The clinical presentation will be held at the Amphitheater, Pratt Diagnostic Hospital, and all other events at Longwood Towers, Brookline.

PROGRAM

- 4:00 p.m. Clinical presentation by the staff at the Boston Floating Hospital.
- 6:30 p.m. Refreshments.
- 7:00 p.m. Dinner.
- 8:00 p.m. The Factors Influencing Dental Caries in New England. Dr. Joseph Volker.

Members of the medical profession and students are cordially invited to attend the evening meeting.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 30

- FRIDAY, DECEMBER 1**
 - 10.50 a.m. Virus Diseases Dr. George Morris (Postgraduate clinic in dermatology and syphilis.) Dowling Amphitheater, Boston City Hospital.
- SATURDAY, DECEMBER 2**
 - *10.00 a.m.-12.00 m. Medical staff rounds. Peter Bent Brigham Hospital.
- MONDAY, DECEMBER 4**
 - 12.00 m.-1.00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.
- TUESDAY, DECEMBER 5**
 - *12.15-1.15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.
- WEDNESDAY, DECEMBER 6**
 - *12.00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

(Notices continued on page xv)

arties under the ordinary law of contract. And in days when any old bargain was held valid, yet to discover a case in which a bungling cian was allowed to get off with a plea of *caveat* or.

e law went to lengths unknown elsewhere to certain that the common health was served. spect to the wares of trade the law of single usually holds; a commodity is available to all wish to purchase on exactly the same terms. nsure adequacy of service, a special rule of law decreed for the physician; he was permitted to ge different fees from patients differently ted. The "sliding scale," as much later it came called, served a definite social end. It elevated cine above commerce, broke the pecuniary action between the doctor's service and his rd, and gave legal recognition to the principle persons were to be served according to their y, that charges were to be assessed in terms of y to pay.

ot so long ago, in my official work, the public acter of the doctor's calling was vividly brought . It is a matter of public record, so I might as confess; I was one of the "small group of will-nen" who instituted the antitrust suit of the ed States against the American Medical Asso-on. The occasion, you will recall, was a boycott of the Medical Society of the District of Columbia ertain physicians employed under a group-h plan. The society had expelled one physician, d a second to break his contract and denied ital facilities to their patients. Now, had the been between rival schools of medical practice, a layman, would not have been entitled to an ion. But both group health and the medical ty stood for orthodoxy; there was no difference . Had the question been a choice between two of many ways of organizing medical service, I d in time have arrived at my own answer. But ould have wanted to get all the facts, examine rience critically and think hard and long before ding. But the issue was far simpler; it was ly a question of a fair field and no favors be-n two rival — and it seems to me immature — s for bringing doctors and patients together. he members of the group, the American Medical ociation seemed to be attempting to keep this : of medical care from having an opportunity rove — or to disprove — its case, and they were nced — the courts have now agreed with n — that the tactics were clearly illegal.

s the case went forward, this notion of medicine he instrument of the common health was the ernment's mainstay. Again and again we had sion to recite the public character of the phy-sion's office. There was a time when an associa-on of doctors acted with the delegated authority he state itself. The Royal Society of Physicians l a charter from the English Crown that con-

ferred on it the right to license, to discipline its own members, to search for and to seize illegal drugs and otherwise as a corporate body to secure the common health. When, much later, Congress issued a charter to the Medical Society of the District of Columbia, it described its rights and obligations in words almost identical with the charter of the Royal Society. But it was careful to withhold from the new medical society all economic power over its members. It refused to confer on it authority to fix any schedule of fees for service; and, to clinch the matter, it stated that the privilege accorded was for scientific and educational work and for "no other purposes" whatever.

The same legal recognition of the public interest marked the law that converged on the case. The American Medical Association — or rather, its attorneys — argued at one time that medicine was not a trade; hence doctors, even as officers of an association, could not be guilty of restraint of trade. And at another time they claimed for the American Medical Association the immunities from antitrust that by acts of Congress have been accorded to the labor unions. If, as the *Journal of the American Medical Association* insisted, it was an insult to call medicine a trade, it is a little hard to see how dignity could be restored by calling its association a trade union. The freedom accorded the unions was intended to make possible collective bargaining with their employers, whereas here a collective bargain between physicians and their patients is just the thing the American Medical Association stood against.

But, just to get the record straight, never once in all the proceedings did the Department of Justice call medicine a trade. Instead, it lodged against the American Medical Association the charge of restraint of trade. Now, "restraint of trade," like a hundred glib medical phrases, is a term of art; one can no more than with a bit of medical nomenclature discover its meaning by looking up its verbal parts in the dictionary. And, as irony would have it, it is medicine more largely than any other calling that has given us this rule against restraint of trade. A doctor sells his practice to another doctor. He covenants that for a period of nine years and within a distance of twenty-five miles he will not engage in practice. For a reasonable time, say two years, he endures his idleness. But the itch to be up and at it grows, and sooner or later the old shingle is hung out. Then the other doctor, who has laid out good cash, becomes indignant, demands what he paid for and calls for justice. The doctor who found that it is not healthy to rust has his ready defense. Society needs his services. The contract he made is in restraint of trade, hence it is void as against public policy.

Sometimes the plaintiff wins, more often the defendant does, but always the court pits the common health against private advantage. The phy-

that up to now has hardly been explored. It will not be solved until we learn to make culture in all its color and drama an instrument of health.

Institutions of some sort must be set up to serve each of the great needs of life. A people must be fed, given laws, protected against the weather, held to a moral code, provided with escapes from the dullness of everyday, fitted out with the comforts and frivolities that make life worth living. As we jog down the centuries and over the globe, the ways in which these great tasks get performed present a most kaleidoscopic picture. If the job be to appease the gods, educate the young, ward off plagues, each people has its own way of doing it. Nowhere is there a final answer; there is always bother and striving that it may be better done.

Now, the health of the people is among the mightiest of these great tasks. Yet the problem of the adequacy of medical care is unusually baffling. For it is only the exceptional person who has experienced all the arts — technical, economic, cultural — that converge in it. A beginning of understanding lies in a recognition of a distinction between the technology of medicine and its organization. By technology I mean all those arts — diagnosis, therapeutics, surgery, radiology, dentistry and the like — that constitute the profession of medicine. By organization I mean all the arrangements, social and economic, by which medical service is made available. It is idle to dispute which is the more important, for there must be a medicine to practice, and there must be some sort of arrangements for bringing physician and patient together. It is no veiled mystery to tell which is the more backward. In the advance of the arts of medicine, the medical profession has done a brilliant job. In the face of this advance it is all the more tragic that progress in the organization of medicine has lagged — and, because of this lag, the nation has not had the full benefit of the profession's superlative performance.

For backwardness in organization I am not disposed to pass out blame. But we should be quite frank in looking into reasons. One must be able to state one's problem before he can solve it, and I wonder whether a primary cause of the backwardness is not a failure clearly to put the question. Is not confusion found in attitude, in approach, at the very beginning of inquiry? To be specific, I profess no knowledge of the practice of medicine, and should I attempt to "lay down the law" as to how to treat an ailment you could — and quite properly — laugh me down. Yet as a group physicians have been little exposed to the discipline of the social sciences, and social organization is as intricate and as full of mysteries as is the art of medicine itself. So that when I hear a physician speaking about the organization of medicine in a tone of doctrinaire finality, I cannot fail to remark the contrast with the courageous and humble search for

truth displayed in his own work. And when I hear the question put as a choice between "private practice" and "socialized medicine," I cannot escape noting a confusion and dogmatism strikingly different from the scientific approach. As for the "either . . . or" of private practice and socialized medicine, there is no such question. There are a myriad of schemes under which the doctor and the patient may be brought together — not a choice between just two.

Here, then, is the main reason for the great lag of organization behind art. Organization must be shaped in the full knowledge of the economic and social arts, yet it also must be shaped to the arts of medicine and the distinctive service it renders. Advance, then, depends on a range of understanding that neither you and your kind nor I and my kind alone possess. It demands a co-operation of professions that is not yet a going fact. As now we take counsel together we are not going to clear up the problem. But this is the kind of thing, multiplied a myriad of times over, out of which will some day emerge the answer to the question of justice and the future of medicine.

* * *

Down through the centuries the common law has recognized the maintenance of "the common health" as one of the great tasks of society. In Europe, and in America, there never was such a thing, strictly speaking, as "the private practice of medicine." From the earliest days the common law has made this clear. It is true that from days of old the doctor held no public office, but his service was — as the judges put it — "clothed with a public interest." At a time when any man — butcher, mercer, wheelwright, baker, fishmonger, candlestick maker — was free to enter the trade of his choice, a license was required of the doctor. To secure his right to practice the candidate had to prove his knowledge, his integrity, his skill. The physician was not free to select or to reject patients at will. As one who followed a common calling he held himself out to serve all in need to the limit of his capacity. No inability to pay a valid excuse for the refusal of his service. The law recognized him as a kind of unofficial servant of the community and exempted him from the ordinary rules of the market. It wisely refused to crowd the relation of doctor and patient into the elementary forms of trade. The doctor rendered a service; the patient, if he was able, paid a fee; but the courts refused to regard the matter as a business deal.

On the contrary, the law judged the relation by reference to the norm of common health. It was recognized that the patient, unversed in the mystery, was unable to judge the quality of service. Hence the doctor, in taking a case, assumed a trust unknown in respect to trade at large. The courts steadfastly refused to bring the rights and duties

lety, and it has not yet been shaped to the circumstances of modern life. In the large cities, and in smaller places, there is something of a trend toward fashionable, middle-class or industrial-maker practice. Here obviously the sliding scale no longer operates, for different physicians serve sons in different income groups.

It is far more serious that charges as a whole are out of accord with the ordinary standard of life. As medicine has advanced, its arts have become more intricate. Yet very little attention has been given toward making up-to-date facilities available at prices the common people can afford to pay. On the whole, it is not that physicians are paid too much; the statistics I have seen lead me to believe that remuneration is quite inadequate. It is rather that there is waste, a failure fully to use facilities, a lack in getting the most out of a trained personnel.

The result is a national tragedy. The rich, who do not have to consider price, are often pampered with a medical care that they may not need. Paupers are often indulged with a service that rises far above the ordinary way of life. The great middle class demands charges on the whole quite above its ability to pay. As a result, a great part of the population is forced to reduce its demand for medical service to the very minimum. A great volume of cases reach the doctors in an aggravated condition that in early stages could have been easily handled. A necessary service is often secured at the cost of a heavy debt — a fact that does not make for health. And a far greater part of the people than I like to admit never come to your patients.

Here, then, is the challenge. The arts of medicine have advanced; the importance of medicine has been enhanced; it has become a necessity to the people and an essential in the operation of the industrial system. It has outgrown the organization into which in days of petty trade it was cast. The demand is for a vaster, more comprehensive, more reliable medical service than exists at present. If an instrument of the common health can be provided on terms the people can afford, the people will rejoice. If you do not help them to it, the people will seize on whatever agencies are at hand as a help. For the universal demand that the common health be served cannot much longer be stayed.

* * *

A new medical order is inevitable. Whether we shall cling to the old or create a new is not the question. The swift course of events has decreed that there can be no turning back. The question is whether what sort of medical order it is going to be, and whether it is the best that wisdom and knowledge can contrive. Like every promising venture, it has its hazards. Is it to be shaped by the best understanding that law, medicine, the social studies,

can bring to it, or is it to be constructed by amateurs in ignorance but with good intentions?

I can understand how, in the face of a new venture, you wonder whether change may not fail to constitute progress. I am certain that there will be serious loss if you sit on the side lines and allow whoever may come to power to shape this new medical order.

As medicine gropes for a new organization, we all hear a lot about the doubts and fears of the profession. Many doctors are fearful lest objectives that have been hard won and that they value highly be lost. Many do not see how things that to them are essential can be fitted into a new order. Let us run through a few of the current perplexities.

A great many physicians are justly fearful that the quality of service will be compromised. From the profession I have frequently heard the argument that when the Government undertakes to look after people's health, the service rendered is invariably poor. With this insistence on quality I fully concur. Nor do I dispute the fact that the new venture may provide a service that fails to meet the standards of the profession. But I cannot follow the argument that a causal relation exists between governmental auspices and poor medicine. The truth is that a new system brings medical care to hosts of people who before have had no access to it. For them there can be no falling off in quality; there has been no service to fall off in quality. But under a new system the provision of doctors and facilities almost always falls short of the new and enlarged demand. As a result, doctors with exacting notions discover much with which they can find fault.

But let us be fair and place the blame where it belongs. The shortcomings are not necessarily due to the new system. They are probably caused by a shortage of personnel and equipment with which to work. It is hardly wise to blame untried arrangements when there is a scarcity of doctors, nurses, clinical facilities and drugs. No system can discharge its obligations if it lacks the men and materials with which to carry on.

Much is said, too, about the maintenance of a so-called "personal relation" between doctor and patient. Like the law, medicine is practiced by persons and is practiced on persons. The patient may be served by one or a number of physicians; the contact may endure for a single call, over a stretch of time or for a long period of years. But in the practice of the profession, there is no escape from a personal relation. The law has made this clear beyond a reasonable doubt. Not so long ago a declaratory judgment was sought in the District of Columbia against the Group Health Association. The action was brought in behalf of the Medical Society of the District of Columbia, which argued that a corporation could not legally engage in the practice of medicine. The Court replied that med-

sician's service is of such public importance that he is not allowed by his own will and to his own advantage to swear away his right to practice. We were able to present more than one hundred cases in which the rule against restraint of trade was applied to medicine. The rule emerged, in fact, very largely out of actions of doctor versus doctor.

With the victory of the Government in the Supreme Court the case is now closed. I advert to it only because it has current significance. It is, to borrow a term from your profession, a symptom of a pathologic condition in the organization of medicine. The organization of medicine has not kept up with its technology. The fault is not individual, but institutional. The cleavage is not to be eradicated by invectives, by isolation from modern thought, by clinging stubbornly to that which was once good. It can be resolved only by an escape from folklore, a probing diagnosis, a conquest of prejudice, a drive at the very heart of the malady.

* * *

Let us briefly survey the great trends that converge on medicine, for they decree a revision of means if the great ends of the Hippocratic Oath are to be served.

First, the art of medicine has refused to stand still. The family doctor — with his bedside manner, his nostrums, his ponderous vocabulary to conceal his perplexities, his downright devotion to duty and sacrifice of self — was once the very epitome of the art of healing. He has been succeeded by the general practitioner, who is a focus to a group of specialists, of which there are now more than a score, each with what a lawyer would call its own jurisdiction. The physician's office, filled with gadgets and contraptions, has become a combination of consulting room, laboratory and miniature hospital. A number of separate shops for x-ray examinations, chemical tests and pathological checkups have become necessary adjuncts. Access to a hospital has become a requisite to the individual physician. Consultation with his fellows has grown into an essential of practice. And behind all this is medicine, which, as science and an art, is on the march. Behind medicine stand optics, physics, chemistry, biology, bacteriology. And still medicine continues to capture provinces that until recently lay beyond its frontiers.

Second, the community that the physician must serve has changed with the times. In the good old days the parson, the squire, the doctor, each held sway over his flock. Allegiance to the family doctor was a tie so firmly rooted that it took a crisis to break it. But the world no longer invites so durable, so personal, so exclusive a relation. The machine, the corporation and the pecuniary calculus have made over our work, our lives, our personal relations. Our society has become urban, industrial, gregarious. We have become a new sort

of wanderers, a race of modern nomads operating a material culture.

For most of us a job has come to replace an equivalent in the old homestead. For most of us livings, no longer taken directly from the farm, are paid between the wages we receive and the prices we must pay. As individuals we are as stubborn as ever our ancestors were. But we act far less on our own and far more as managers, agents, employees. Our industry is operated by corporations; our farmers band themselves into co-operatives; our workers skilled and unskilled, gather into unions; even the great mass of our scientists make their discoveries while working for others. In our culture the group has come to be the regular thing.

Against such forces our minds cannot stand firm. Profound changes in habit, interest and value have come in their wake. The standard of living has moved to a place of primacy among our everyday concerns. It makes the costs of medical service an inescapable problem. The care of the sick can no longer be absorbed by the family; it becomes an item of expense in the budget. If it is a wage earner who is ill, there is a double cost: absence from work means loss of earnings, and bills are there to be paid. So medical service becomes a sheer economic necessity, for unless a man's capacity to work is maintained, he ceases to earn. Health thus becomes an aspect of the operation of the national economy.

And within this urban, industrial, wage-earning society, men and women are becoming increasingly conscious of what they want. Our workers demand health as a condition of their livelihoods. They insist on adequate medical service at a price they can afford to pay, and in their newly won self-respect they will refuse all charity.

Third, a changing medicine has not yet been adapted to its new world. The high objectives of the profession endure, for they are eternal, but they must be freshly applied. Our society cannot be served by an instrument designed to fit the family physician into the village community. Neither my time nor your patience will permit a prolonged analysis, yet two or three soundings will reveal the nature and contours of a very insistent problem.

In the not so long ago the old-fashioned doctor could be depended on to administer medicine for the community. He could see to it that needs were met, service was adequate and costs were justly distributed. The physician of today is in no position to discharge this office. His practice comprehends not the whole community, but a mere fraction of it. If he is a specialist, the fraction is highly selective. And the whole body of physicians, each operating by himself, has no collective instrument by which it can apportion the totality of service in accordance with general need. Nor can it any longer take the specific responsibility of graduated charges. The sliding scale survives as a legacy from a simple

ety, and it has not yet been shaped to the circumstances of modern life. In the large cities, and in smaller places, there is something of a trend toward fashionable, middle-class or industrial-like practice. Here obviously the sliding scale no longer operates, for different physicians serve persons in different income groups.

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The result is a national tragedy. The rich, who do not have to consider price, are often pampered with a medical care that they may not need. Paupers are often indulged with a service that rises far above the ordinary way of life. The great middle class is charged on the whole quite above its ability to pay. As a result, a great part of the population is forced to reduce its demand for medical service to the minimum. A great volume of cases reach the doctors in an aggravated condition that in early stages could have been easily handled. A necessary service is often secured at the cost of a heavy debt — a fact that does not make for health. And a far greater part of the people than I like to admit never come to your patients.

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can bring to it, or is it to be constructed by amateurs in ignorance but with good intentions?

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A great many physicians are justly fearful that the quality of service will be compromised. From the profession I have frequently heard the argument that when the Government undertakes to look after people's health, the service rendered is invariably poor. With this insistence on quality I fully concur. Nor do I dispute the fact that the new venture may provide a service that fails to meet the standards of the profession. But I cannot follow the argument that a causal relation exists between governmental auspices and poor medicine. The truth is that a new system brings medical care to hosts of people who before have had no access to it. For them there can be no falling off in quality; there has been no service to fall off in quality. But under a new system the provision of doctors and facilities almost always falls short of the new and enlarged demand. As a result, doctors with exacting notions discover much with which they can find fault.

But let us be fair and place the blame where it belongs. The shortcomings are not necessarily due to the new system. They are probably caused by a shortage of personnel and equipment with which to work. It is hardly wise to blame untried arrangements when there is a scarcity of doctors, nurses, clinical facilities and drugs. No system can discharge its obligations if it lacks the men and materials with which to carry on.

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icine can be practiced only by physicians and that the Group Health Association, a corporation, did no more than furnish the auspices under which physician and patient were brought together. Whatever the character of the organization, the relation is in essence personal.

An oft-repeated variant of the same theme is the insistence on the right of the patient freely to choose his physician. As a patient I am quite willing to have this right qualified for my own good. A well-recognized principle of economics has it that freedom of choice should be limited where the consumer is not a proper judge of the quality of the ware. If there is one field where freedom of choice should be qualified, it is medicine. For medicine is not one thing but many things. Its services are of a highly technical character. If we are downright honest, you and I know that the layman possesses neither the facts about the distinctive competence of particular physicians nor trustworthy norms to guide his judgment. In a matter of medicine, I am not foolish enough to trust my own choice — and a check with some of my lawyer colleagues indicates that they agree with me. I have over the years, through the devious ways by which a layman gets a little practical knowledge, discovered a physician or two whose judgment I have reason to trust. And with me it is their choice, not mine, that goes.

How many patients have walked into your office whose ailments have been aggravated by an amateur's choice of a physician? If for a moment I can be quite rash, I venture to say that in medicine, competence does not wholly accord with ability to attract patients, as in law it does not always rest on ability to attract clients. List, if you will, the six physicians in your city in whom you repose the greatest confidence. Let me, from the records of the Bureau of Internal Revenue, list the six who have the highest incomes. It is dollars to doughnuts that the lists do not match. People go to the Johns Hopkins Hospital or the Mayo Clinic not to be treated by a particular doctor but to secure skillful service. A personal choice, for that matter, can be secured even under state medicine. But far more important to the patient is the assurance of a high standard of competence.

Nor is wide-open freedom fair to the physician. He should on sheer merit advance in his profession, but in all justice his work should be judged, not by the laity, to whom medicine is still a mystery, but by men of his craft, who can distinguish brilliant from routine work. "The free choice of a physician," I fear, has become a shibboleth that will not stand analysis.

And candor compels me to say that I feel much the same about the argument that group practice robs the physician of his incentive. In its usual form it runs that if a man is on his own, he will give his best; if he works for a salary, he will put in his hours and let it go at that. The age-old traditions of your

honorable profession deny the truth of such an argument. Your code of medical ethics has always elevated the relief of suffering above the pursuit of gain. Its purpose has always been to save the physician from avarice, one of the seven deadly sins. It has long been a canon of yours that service is to be given to rich and poor alike, that quality is not to be tempered to the ability of the patient to pay. My limited experience indicates — and a number of colleagues to whom I have put the question concur — that the mightiest urge to which the physician responds is the pride, the drive, the keeping faith with his calling. A doctor cares, and cares mightily, about the respect of his fellows. A friend of mine tells me of his oculist, who insisted he should stop in Baltimore and consult an oculist there. My friend, professing himself satisfied, saw no occasion for the consultation. Finally the oculist said: "Do I have to be brutally frank? I'm damn proud of that operation on your left eye; Doctor — is my old teacher, and I want an excuse for him to take a peek at my work." You know better than I that a conscientious and resourceful physician is not, if he can help it, going to allow a case to lick him. And, if the case is tough and he loses, it hurts.

Now, I do not say that material things are to the doctor of no account. Like the judge, the lawyer, the engineer, the university professor, he has a right to demand advancement, security, an income adequate to his standard of life. For the professional man such things are necessities. Without them the physician is not in a position to give his best.

But such values depend on no single way of organizing medicine. To say that a doctor will give his utmost if he acts as his own business agent, and that his incentive will be stifled if he receives a salary, is not borne out by experience. The time was when the great scientific advance was the work of the solo inventor. Today the most creative of all work — the progress of science and the useful arts — is the product of men on salary. In the large offices the great mass of lawyers now work on salary, and work as hard and as heroically as the youngster who used to flaunt his own shingle in the breeze. It is true that the chance to become a partner is a prod, but I should not rank it overly high, for work equally as good is done by the lawyers in the Government, where no such opportunity exists. In our institutions of higher learning, research as well as teaching falls to salaried employees, and there you will observe an interest, an excitement, a devotion to duty, an urge to be up and doing. And, to return to medicine, how many thousands of our best doctors are today giving their all without stint in the service of the Army and the Navy?

Ambition, security, income, are necessary things. They have in every age and among the most varied conditions of society driven men to accomplishment. If I were a youngster, I should rather leave the series of judgments that shape my career to men

my own profession than attempt to get ahead translating my skills into the art of winning and losing patients. And, most important of all, why, I ask you, that doctors are troubled by this at when university professors, lawyers in public life, officials who make of government a life-style, never even raise the question? And why is that, when the Government of England first undertook to offer medical service, there was quite a chorus that viewed with alarm the loss of income, whereas today such a doubt remains unvoiced? Is it so easy enough to answer the argument that a state will kill the urge to serve; it is hard to understand why the question is ever asked.

It is too late to turn away from that fearful substitution of the state as employer, for I am already disliking it. As for myself, I have no more fear of a venture of the state into medicine than I have of a venture of the state into law. The venture into law is old — judges, public counsel, prosecuting attorneys, are examples. The venture into medicine — pauper and the criminal aside — is new. But the traditions and high standards that have long prevailed in one realm can be established in the other. The Government, in most of its activities, has adhered to a very high standard of professional competence. If for a moment I may be personal, I have experienced the practice of law in a large private New York office and in the Department of Justice. The Government has never imposed on me the restrictions that I have felt to be a burden. If anything, I have enjoyed a greater freedom than I could have had in a private law office. It is true that frequently my own judgment is tempered by the opinions of my colleagues, but usually a "consultation" — as you call it — leads to a sounder decision than any one of us alone would make.

You are right in insisting that high standards of medical care must not be compromised, but standards are a professional matter. Their chief dependence is on adequacy of resources. They are not inherent in any type of organization. Your current efforts, as well as state medicine, have their insidious dangers. And, since comparative merits are at issue, I am not content with any argument that points out the faults of the one without looking at the faults of the other. As it is now practiced, medicine is exposed to the corroding ways of business. Witness the exposure of fee splitting in the City of New York. Under another dispensation it may be exposed to the strange ways of politics. Which is the greater temptation, I am not able to say. But politics is a thing from which no activity of man is free. It can be employed to achieve holy as well as unholy results. And the state is not, as some of our physician friends seem to fear, a ward heeler leading the doctor how to practice.

I am not, mind you, presenting a case for or against the prevailing system, state medicine or any particular medical order. There is, as I said

in the beginning, no such question as "private practice" versus "socialized medicine," for practice is never private and all medicine has a social function. The question you and I face is harder, more intricate, far more detailed, than any such antithesis suggests. First of all, you must ask what you want medicine to do. That is easy: to furnish to the whole population an adequate service of quality on terms it can afford. Next, you must contrive ways and means for seeing to it that the great variety of services we call medicine are called into play to serve the common health. Next, you must set up protections against the hazards that you and I see so clearly. And finally, all these arrangements must be brought together into a going organization. Such a result is not to be attained by an act of faith or a single trial. The conditions of health vary from city to country, from section to section. The needs of the people as locally felt must be met, and this means variety, flexibility and capacity for adaptation. It means, seek — honestly, objectively, courageously and ye shall find; knock at many doors until the right ones shall be opened to you.

* * *

Thus there is no royal road to a modern medical order. And thus the system we seek is no choice between "private practice" and "socialized medicine." For in following his private calling the physician is fulfilling a social service; in medicine, "private" and "social" have always been and always will be associated. And the terms, so frequently set down as opposites, have only the most evasive content. Private practice has no stabilized form; the private practice of the country doctor who rode his nag, did his rounds, was monarch of all he surveyed, is not the private practice of a modern urologist. And socialized medicine embraces systems as distinct as the charity of the medieval church, the Royal College of Physicians, the clinic of a modern university, a bureau of public health and the Russian way. You can no more get anywhere with such terms than you can practice your profession with a general concept of "disease" as your stock in trade.

The question demands, not an easy answer, but painful, constructive, detailed thought. It demands, too, an indulgence in downright trial and error, without which nothing worth while emerges. A few experiments — far fewer than the length and breadth and depth of the subject demand — have been blazing fresh trails. An increasing number of physicians have enjoyed practice on their own and on salary and are prepared, from experience rather than in speculative terms, to assess debits and credits. In my pocket I have a letter from one such physician who sets down an illuminating comparison by no means to the disadvantage of salaried work.

And, last but most important of all, the war has given a quick step to a trend long in the making.

A host of physicians now in service are conscious of the shortcomings of "military medicine" and have scores of suggestions concerning how it can be improved, but they have become aware of the tremendous possibilities that inhere in a medicine directly organized to perform its function. And millions of soldiers, returned from the front, are going to demand for themselves and for their families the instruments of health to which they are entitled.

The course of events moves fast, and to me a new medical order seems inevitable. My fear is not that we shall not get it—an awakened public, sparked by our veterans, will see to that. My fear is that we shall not bring to its creation all the knowledge, wisdom, understanding we possess. A reference to the Wagner-Murray-Dingell Bill will make my point. About its intent and objectives there can be for me no dispute. Its detail of provisions, however, may or may not fall short of its purpose—I do not know. On ways and means I am open to argument in behalf of something that is better. In respect to the necessity of distributing the cost of protection against ills I am wholly convinced, and I think the American people is adamant.

The medical order that our stalwarts defend has already ceased to exist. A new medical order will come to be even if we do not will it—even, in fact, if we stubbornly resist it. For the medical order, like other institutions, cannot insulate itself against the impinging culture. It must make its response to the great pulsing tides that everywhere else enter our national life. The wiser physicians know that sheer opposition is not going to hold back the tide. They are putting forward—it seems to me a little timidly—proposals of their own. The other day the medical society right here in St. Louis voted approval of a plan for prepaid medical care, and the papers stated that a minority of doctors thought it did not go far enough. Timidity must be replaced by high resolve, and I am afraid that a very old adage that goes back at least as far as ancient Egypt applies here: "If you can't stop a movement, join it."

And, quite seriously, the doctors' joining is essential to the movement's salvation. The organization of medicine is an affair of a couple of shops. It is a job for the craftsman in social order, but it must be shaped to the very life of the medical service it has to offer. If doctors oppose, or stand on the side lines, the layman will create a medical order that may prove to be indifferent or even blind to the values doctors prize most. If the doctors assume a role in creation, they can see to it that no compromise is made with the standards of the profession.

The problem thus becomes one of creation. In respect to a long detail of questions—the selection of personnel, the standards of care, the carrying of risks, the methods of payment, the ways of remuneration—a score of ways are open. The form of organization may follow an agency of state,

the university pattern, the hospital setup or a combination of devices derived from all these. The government may dominate the system, become one of a number of parties to its management or be excluded from it altogether. The venture may fall into the legal form of a public-health authority, nonprofit-making corporation, a series of independent or interlocking corporations, a group of consumers co-operative, a mutual association of the profession and the laity or still something else. Its direction may be lodged with a tripartite board representing the government, the public and the profession, or the public and the profession, free from governmental interference, may assume joint responsibility. It may or may not be state medicine; it cannot escape being social medicine.

It is man for whom medicine exists. Its function must be to keep a whole people in health. The doctor must be the focus, but on his office a host of unlike services must converge. He must not stop with asking, "Of what is this man ill and what can I do about it?" He must also inquire, "Why and how did this man become ill in the way he did?" The quest leads beyond cure to all the conditions on which personal well-being depends. For food, clothing, housing, recreation, family, occupation, social life, are all terms in the equation of health. Nor must man's habitat be forgotten, for adaptation is the requisite of the life process. Many arts must converge into the new medicine; prevention, sanitation, the public health, must become a part of it. At its hub must stand the doctor; it is he who must direct this vast apparatus of skills, specialized personnel, facilities to the service of the human being. The medical order that I suggest—and that which the American people are going to have—will be vaster and mightier than anything we now know.

Such a medical order, it seems to me, should be hailed enthusiastically by the physician. In respect to professional matters his word will go. His opportunities for service will be greatly enlarged. He will have access to facilities that only the exceptional physician can now afford. A shift in work now and then will keep him alive in his profession. He can occasionally get away for further training. And above all he ought to be better able to turn his clinical work to permanent account.

In an abstract way I recognize the values of ivory-tower research. But after all, the heat of the daily round has its own contribution to make. In the last five years Antitrust Division of the Department of Justice has perhaps done more to blaze a path for the law than has any law-college faculty in the land. The result has not been due to any unusual ability of the men in this division; they have simply been on the firing line and have had an opportunity to turn their clinical work to account. To me it seems that one of the great shortcomings of the prevailing medical system is that the practitioner is kept so busy with his patients that he

not translate his work into medical discovery. Thus, in the end, I return to my beginning. I can find you no ready-made medical order on a silver platter. If I could, it would do you no good. I can only suggest to you, whose minds have long been busied with the subject, some reflections of a man of another profession. And I am positive that a service adequate to the times cannot be brought into being without the doctor's creative participation. As doctors and patients we face a crisis, and my appeal is to the ancient wisdom of the profession. The ends of medicine remain un-

changed; ways and means must be found to adapt its practice to the conditions of present-day society. A new organization must be created that an ancient mission be not lost, that once again medicine shall be available to all in need and that charges shall be graduated in accordance with ability to pay.

An instrument of the common health, such as never before has been offered to a people, is within our reach. This is no time for petty doubts and timid moves. In the face of a national challenge we must — as one of our great jurists said of the law — let our minds be bold.

A UROLOGIST LOOKS AT CHANGING TRENDS IN MEDICAL PRACTICE*

HERMAN L. KRETSCHMER, M.D.†

CHICAGO

WHEN your president invited me to take part in your program and suggested that I talk on this subject, I wondered what he had in mind. Does the urologist who looks through the cystoscope have a point of view different from that of any other practitioner of medicine? I believe that he should not have. After all, these social trends are of vital interest and importance to every physician in this country, be he general practitioner, specialist, research worker or teacher.

"Public health is the musical instrument easiest for the welfare worker to play, and the softest chord is the venereal problem. They not only are able to stir the sympathies of the public, but also can arouse it to supporting the movement through fear of infection." Thus spoke Dr. James A. Gardner in his chairman's address before the Section of Urology at the seventy-third annual session of the American Medical Association held in St. Louis just twenty-two years ago. He was one of the first among our members to interest himself in the early manifestations of these beginning social trends.

It is interesting to reflect that at this annual session of the American Urological Association in St. Louis, a part of the program is being devoted to a consideration of social trends from the urologist's point of view. Unfortunately, many specialists have been indifferent to impending social trends. Their aloofness to the many problems of medicine and their lack of interest in the work of their county and state medical societies and in the activities of the American Medical Association are difficult to understand. This is not to say that they have not been interested in their respective special societies, both local and national. The specialist and his special society have

done much toward improving his type of practice and increasing the scope of knowledge along his own line, and have contributed to the training of future specialists and to the rendering of better medical care to the people of this country.

No one will say that this great organization has not met all its obligations in the fullest possible manner, and no one will question the statement that nowhere in the world is urology on so high a plane as it is in this country. Nor will he deny the statement that the people of the United States receive the best urologic care that it is possible to obtain — and this under the present system of practice, without regimentation and socialization. I should, however, like to have each member of this association ask himself these questions: How many times have I attended my county medical society meetings in the last five years? How many meetings of my state and the national association have I attended? What have been my contributions to the work of the American Medical Association and its component societies, besides the presentation of scientific papers?

I am reminded of Dr. Frank Billings's statement made to me in Dallas at the meeting of the American Medical Association in 1926. He told me that he had been a member of the association for forty-five years and had attended forty-four annual sessions. This is an example to be followed by every physician in this country.

I should like to point with pardonable pride to the activities of some of our colleagues in the House of Delegates of the American Medical Association. Although I cannot mention all of them, I should like to mention some of the old wheel horses who have taken an active part in this representative body: Abell, Bandler, Braasch, Cameron, Crockett, Hamer, Low, Parke, Sargent, Smith, the late Terry Townsend and others. In my travels throughout

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†President, American Medical Association.

the country I am pleased to see more and more urologists taking an active part in their county and state societies.

Unfortunately, in this country there is a fetish for passing laws. People seem to think that by simply passing a law all will be well. And they never seem to learn. Note the miserable failure to regiment the drinking lives of the people represented by the Volstead Act. No disease is cured by the passing of a law. Diseases are cured and eradicated by research, medical education and treatment, and not by regimentation. All the laws on the statute books failed to eradicate venereal diseases, but now, as you know, effective drugs are available. I recently heard Admiral McIntire state that the venereal diseases are no longer a problem in the Navy. When, as a result of medical education and research, specific remedies have been discovered and their use by physicians has been established, and when their use does not entail a protracted period of treatment, the co-operation of the patient is readily obtained and the results are almost miraculous.

The regimentation of the people and the physicians has never solved any medical problem. Unfortunately, regimentation only makes matters worse. The various attempts to regiment the medical profession are only a steppingstone in the regimentation of the entire country. Many citizens are now keenly aware of the dangers that will follow such a procedure if applied to the medical profession. Once the medical profession has been regimented, the other professions, as well as commerce, industry, newspapers, communications and other activities, may share a similar fate. Note, if you will, the detailed study given to the Wagner-Murray-Dingell Bill by the American Bar Association.

I do not need to call your attention to the fact that under regimentation medical education and research always suffer, that the quality of medical service to the patient deteriorates and that the cost of the service always goes up owing to an ever-increasing bureaucracy. Some years ago from 51 to 53 per cent of the payments into the *Kranken Kassen* in Germany went for administration and the remainder for all phases of medical care.

Under the present system of practice in the United States the span of life has been increased to sixty-five years; maternal deaths have reached an all-time low despite the fact that over 3,000,000 babies were born last year and that over 58,000 physicians were in the armed forces. Infant mortality was never so low. Diphtheria, typhoid fever and other acute infections are practically nonexistent. Tuberculosis, which has always shown an increase in

every war and after it, has also reached an all-time low. Surely the physicians of this country can be proud of their achievement. It behooves the people to stop, look and listen before they abandon the type of practice that has given them the best medical care possible. Do the "do-gooders" believe that they can improve on the results?

There are isolated areas in this country in which there is need for the extension of medical services, and the medical profession has always been and is now ready to improve such situations. These needs are purely local and can be taken care of on a local basis. Because of these local problems, which can be corrected, there is no justification for abandoning completely the finest medical service in the world.

It is incumbent on every physician to acquaint his patients with the dangers of the regimentation of medical practice. Every physician must devote a certain amount of time every day to informing his patients just what this means in the way of deterioration in the quality of medical care, the limitation of his choice of physician and the increased cost in the form of increased taxes. I believe that once the patient has been educated so that he understands the implications, he will be loath to give up the best medical service that any nation has ever enjoyed.

The medical profession has never been static. It is keenly aware of the importance of increasing the distribution of good medical service to all the people. In order to study this problem, the House of Delegates recently established the Council on Medical Service and Public Relations to study and analyze the various plans that are now in operation and to make available the highest quality of medical care to all the people. Many of you no doubt are familiar with these various plans, and I need not discuss them with you. Not only is the medical profession interested in this subject, but industry and the insurance companies have given this subject much study and consideration.

I believe that it would be most fitting to express a word of greeting in the form of a message to the members of this society who are now in the armed forces. From the letters of a good many who have written to me, they are wondering what kind of world they are coming back to. It was the impression of the 58,000 doctors who went into the armed forces that they were fighting to free the world of regimentation, in other words, to free the world of dictators and to preserve the American way of life.

The question of regimentation of the medical profession and the patient is one that concerns every physician as well as every citizen of this country.

MEDICAL PROGRESS

CARDIOLOGY: THE NORMAL HEART IN OLD AGE*

A. STONE FREEDBERG, M.D.,† AND HERBERT D. LEWIS, M.D.‡

BOSTON

OR some time the aging of the population has been a matter of concern to many. In 1940 approximately 9,000,000 persons, or 7 per cent of population, were sixty-five years of age or over,¹ whereas a study of the trends indicates that in 1980 approximately 22,000,000, or 14 per cent of the anticipated population will be sixty-five or more years of age. This proportion will be reached earlier in some countries, owing to the excess of young manhood in the present war. It is of importance that life expectancy, for the increasing number of persons reaching old age has increased since 1900 (Table 1). Thus, al-

concerning which changes constitute disease and which are those of normal senescence. It is the purpose of this review to summarize the accumulated knowledge bearing on the normal heart in the aged.

ANATOMY

Heart weight. The absolute weight of the heart is said to diminish with age,²⁵ although the ratio of heart weight to body weight increases, according to Muller²⁶ and Gray.²⁷ Other authors, including Sagebiel,²⁸ point out, however, that atrophy does not occur. Rosahn,²⁹ in a study of 187 men with normal hearts at autopsy, found a significant correlation between age, body weight and heart weight. He derived the formula: age (in years) plus 3 times the body weight (in kilograms) plus 100 equals the heart weight. He concluded that a diagnosis of cardiac hypertrophy was justified when the observed heart weight exceeded by more than 77 gm. (approximately 20 per cent of the mean weight for the entire group) the estimated heart weight. Willius and Smith,³⁰ using a height-body weight method for estimating the normal, found approximately one third of a group of 376 patients seventy to ninety-nine years old to possess hearts with normal weights. In the remainder the excess cardiac weight could be explained as consequent to disease processes, such as hypertension, aortic stenosis, adherent pericarditis and myocardial infarction. It should be pointed out that their upper limit of normal weight is low (294 gm. for males, and 250 gm. for females).³¹ It is apparent that there are as yet too few data concerning normal heart weight in the older age groups to permit a conclusion concerning the occurrence of hypertrophy as part of the aging process unrelated to disease.

Gross changes with age. The pericardium tends to become opaque, particularly over the surface of the base of the right ventricle. The apical portion of the left ventricle is said to decrease in size.³² Subpericardial fat tends to increase along the grooves of the coronary vessels, especially in the auriculo-ventricular groove at the base of the right auricle. The valves become more rigid; calcium may be deposited in the mitral and the aortic ring, with calcification of the annulus fibrosis. The sinuses of Valsalva become deeper. Karsner³³ has pointed out that the latter changes may be due to earlier inflammatory disease, with a loss of its identifying

TABLE 1. *Expectation of Life for White Males in the United States (adapted from Dublin²).*

AGE	EXPECTATION OF LIFE			
	AT BIRTH	AT AGE 50	AT AGE 60	AT AGE 70
35	37	37	37	37
45	48.25	20.76	14.35	9.05
55	62.60	21.08	14.36	9.05

though more men and women in this country are living longer, they succumb to invalidism² and die at rates that have been unaffected by general medical progress.

Although the general social aspects of this situation^{3,4} need not be discussed here, it is apparent that methods of prolonging the period of productivity of the aging population are becoming increasingly important. This involves further studies of disease in the aged, in order that preventive medicine⁵ and active therapeutics may be applied. Studies related to old age have been recently undertaken on a large scale,^{6,7} and books,⁸⁻¹³ a journal¹⁴ and symposiums¹⁵⁻¹⁸ devoted to gerontology and geriatrics have appeared.

It has long been known that death from gradual decay is extremely rare and may indeed be nonexistent.¹⁹⁻²¹ Diseases of the cardiovascular system constitute the main cause of death in the aging. Statistical statistics indicate that heart disease is responsible for 25 to 50 per cent of all deaths,²¹⁻²³ and autopsy data are in agreement.²⁴ Many excellent contributions to knowledge of the heart in old age have been made in the past few years, but a basic difficulty in most studies of this sort is the decision

*From the Medical Service and the Medical Research Laboratories, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

†Assistant in medicine, Harvard Medical School; junior visiting physician and associate in medical research, Beth Israel Hospital.

‡Assistant in medicine, Harvard Medical School; associate in medical research, Beth Israel Hospital.

features. Willius and Smith³⁰ found 93 per cent of hearts from 381 persons aged seventy or more to present varying degrees of valvular sclerosis, so that these changes should be considered normal. Calcific aortic stenosis^{34,35} and mitral stenosis of rheumatic origin³⁶ have been reported in elderly patients who reached advanced ages without suffering any ill effects from their previously acquired valvular disease.

Microscopic changes with age. The microscopic changes of involution have been well summarized by Warthin³⁷: there is a loss of power of cell division with fewer mitoses, a quantitative atrophy with fewer and smaller cells, condensation of the chromatin of the nucleus, nuclear pyknosis, vacuolation and karyolysis, and lipoid deposition in the cytoplasm may be observed. It should be stressed, however, that such changes are usually most marked where the blood supply is insufficient.³⁸ The striations tend to disappear about the nuclei, and an increased amount of pigment may be observed at the poles of the muscle cells. The conducting system is unaffected by the general atrophy. Hyaline fibrosis, with a loss of water, is said to occur, but Hastings et al.,³⁹ studying the water content of the left ventricular muscle in puppies and adult dogs, found no differences. Miller and Perkins⁴⁰ showed an increase in thickness of the left atrial endocardium and a striking increase in elastic tissue fibers, mainly in the auricles but also in the ventricles. Finally, vascular changes such as atherosclerosis, loss of elastic tissue and muscle cells, and calcium deposition are frequent.

Coronary arteries. Whether arteriosclerosis is to be regarded as a senescent change or due to some disease of unknown origin is unsettled. Hirsch and Weinhouse⁴¹ point out that even when only the media of the aorta are taken (avoiding adventitia and the variation with disease in the intima), there is an increased percentage of lipids, particularly cholesterol esters, with age. In a study of routine blood cholesterol and cholesterol esters in 150 persons with a mean age of seventy-seven, 60 per cent had levels higher than 200 mg. (40 per cent free).⁴² The lipid deposits in atherosclerosis seemingly result from nonselective deposition of plasma lipids. It is, however, peculiar that cholesterolemia such as is seen in diabetes mellitus or totally thyroidectomized individuals may be associated with normal coronary arteries. The absence of arteriosclerosis in the Chinese, who not only eat a low cholesterol diet but, as Snapper⁴³ points out, have low blood cholesterol values, may be explained in part by the age of the patients studied.

Whether or not coronary arteriosclerosis is a disease, it is a striking fact that occlusions are found in 40 per cent of males over fifty-five years of age. Thus, as age is prolonged, there is a tendency for completely healthy coronary arteries to become

fewer and for progressively severer changes to appear.⁴⁴ In Akerson's⁴⁵ series the peak of frequency of disease was found in the ninth decade in men and in the eighth in women. On the other hand, healthy coronary arteries are not unusual in old persons.⁴⁶ The development of anastomoses does not occur with progressive age, and this may explain in part the increased mortality in initial attacks of myocardial infarction in old persons. It is of some interest that no correlation between changes in the radial artery and coronary-artery disease exists⁴⁷; in marked cases of the latter the radial arteries may present a minimal degree of arteriosclerosis, both anatomically and clinically.

PHYSIOLOGIC CHANGES

Pulse rate. The pulse rate is said to increase slightly in persons above the age of sixty-five.⁴⁸ Humphry⁴⁹ noted an average pulse rate in women over eighty of 78 to 79, while in men it was 73. In 52 centenarians the average pulse rate was 74 to 75.

Carotid sinus. The carotid-sinus reflex becomes more sensitive with age.⁵⁰ Sigler⁵¹ has attempted to use the degree of sensitivity as a test for the presence of coronary-artery disease and angina pectoris. Although it is true that many patients with angina pectoris have a sensitive carotid sinus, approximately a third do not.⁵²

Cardiac output. Lewis⁵³ found no change in cardiac output in 100 men aged forty to eighty-nine. Thus the mean cardiac index, the cardiac output (in liters) divided by the surface area (in square meters), was 2.3 in the eighth and 2.2 in the ninth decade respectively. Two persons aged ninety-one and one aged one hundred and one had indices between 2.0 and 2.3. The small decline is due to a drop in oxygen consumption in the aged. Previous observers had noted in older persons a lessened oxygen consumption.^{54,55} The normality of the cardiac output at rest is, however, no index of the heart's ability to act under stress.

Vital capacity. Several studies on the effect of aging on the vital capacity show that this measurement is only slightly decreased from forty to fifty years, with a rapid and progressive decline in the older age group.⁵⁶⁻⁵⁸ Thus the vital capacity of otherwise healthy men in the ninth decade of life is found to be about half the accepted standards.^{56,57} A similar decrease in older men occurs in total lung volume, with a concomitant increase in residual air and mid-capacity (functional residual air).⁵⁹ The alterations in respiratory dynamics are a reflection of other changes in structure and function that occur with aging, namely, degenerative changes in the thorax and spine, with limitation of respiratory excursion, obesity and elevation of the diaphragm and loss of elasticity of the lung parenchyma and bronchial tree. If these anatomic changes are accepted as part of the process of normal aging,

in the changes in respiratory measurements that they produce must be interpreted as normal, and standards must accordingly be corrected for age. This is essential for the clinical interpretation of these measurements, since the changes of aging of cardiorespiratory disease are in the same direction.

Acid-base balance. There are no significant changes in acid-base balance. Thus 33 of 50 persons aged seventy or over studied by Dogliotti and Pitts⁵³ had a normal blood pH. The remainder showed changes in pH to the side of either uncompensated acidosis or alkalosis. With exercise old persons, however, there may be an abnormal accumulation of lactic acid and a decrease in alkaline reserve,⁵⁴ indicative of an inadequate increase in cardiac output during exercises, that is, diminished cardiac reserve.

Venous pressure and circulation time. The venous pressure is normal in the aged.^{60, 61} The circulation times, as measured with the fluorescein⁶² and indigo⁶¹ methods, show a definite trend toward lower rates with increasing age, but they remain within the normal upper limit of 20 seconds. On the other hand, the velocity of blood flow through the lungs shows no constant relation to the age of the patient.⁶³

Velocity of pulse wave. Studies of the pulse wave velocity of the radial artery and the aorta showed an increase with age.⁶⁴⁻⁶⁶ This is associated with an increase in elasticity, which may be halved at the age of sixty.

CLINICAL EXAMINATION

False diagnosis of heart disease. A diagnosis of congestive heart failure in the aged based on dyspnea, slight cyanosis, basal rales and a palpable third edge is too frequently made. Pulmonary diseases such as emphysema, pulmonary fibrosis, and chronic bronchitis and atelectasis are, on the contrary, much oftener responsible for these symptoms and physical findings. Peripheral edema, particularly that occurring as an isolated finding, is more usually due to nutritional deficiencies, varicose veins, intra-abdominal tumors and obesity than to congestive heart failure. Chest pain, consequent to cervical or thoracic osteoarthritis, hiatus hernia or gall-bladder disease, is too frequently labeled angina pectoris. A careful history usually all that is needed to differentiate these conditions.

Heart size. A normal-sized heart, although it does not exclude the presence of coronary-artery disease and angina pectoris, does rule out most other forms of cardiac disease. In the aged it is difficult, however, to be sure of the heart size by percussion and palpation. Emphysema probably poses the greatest difficulty in this regard. A markedly hypertrophied heart, as evidenced by an impulse beyond the midclavicular line or a

corresponding left-border dullness, is not normal. Dullness to the right of the sternum may be evidence of enlargement or dilatation of the right side of the heart. An abnormal band of dullness at the base (over 6.0 cm.) is evidence of ectasia of the aorta.

Heart tones. The heart tones are decreased in loudness in the aged.⁶⁷ Emphysema probably plays a role in this phenomenon, although Garguilo and Allende⁶⁸ say that there is a physiologic decrease in the intensity of the heart sounds in old age. Changes in the tones, such as accentuation and disappearance of the second aortic tone, have the same significance in the aged as in younger persons. Accentuation of the second pulmonic sound is indicative of pulmonary hypertension.

Heart murmurs. It is apparent from a consideration of the anatomic data previously cited that soft systolic murmurs at the mitral or aortic area might be expected to be heard in many older people. A loud mitral systolic murmur, however, must be interpreted as due to dilatation of the mitral ring, secondary either to ventricular dilatation or to changes in the mitral valve; an apical diastolic murmur is, as in younger persons, diagnostic of mitral stenosis. Aortic stenosis, a frequent lesion in the elderly, may be diagnosed when two of the following three signs are present: a systolic aortic murmur over the aortic area transmitted to the neck or precordial area, or both (calcium deposits are said to produce a rasping or musical quality to the murmur); a systolic thrill in the aortic area that may be brought out by bending the patient forward; and an absent or diminished second aortic tone. Willius⁶⁴ has divided calcareous aortic stenosis into four grades anatomically and clinically. A division into only two groups is probably more useful. The severe grades of calcareous aortic stenosis showed marked cardiac hypertrophy: a loud, rasping systolic murmur heard over the entire thorax and loudly transmitted to the carotid arteries, a coarse systolic thrill anteriorly in the second and third right interspaces, an absent second aortic tone, an aortic diastolic murmur in a third of the cases and, if aortic insufficiency and hypertension are absent, a small peripheral pulse and low pulse pressure. The milder grades of calcareous aortic stenosis presented a rough and fairly loud murmur heard best in the aortic region and transmitted usually into the carotid arteries. There was usually no accompanying systolic thrill or change in the aortic second tone, and cardiac hypertrophy was slight or absent. It should be stressed, however, that these findings were based on hearts showing definite calcareous aortic stenosis and were not compared to the findings in patients presenting only atheromatous changes in the aorta and aortic valve or annulus fibrosis. A systolic-diastolic murmur and thrill may occur in arteriosclerotic aneurysms and senile ectasia of the thoracic aorta.⁶⁹

but may be differentiated by the presence of a good aortic second tone and by x-ray visualization.

Rhythm. The heart rhythm in the aged is normal. Although extrasystoles do occur, there is no clear evidence that they occur more frequently in the aged than in the young. Paroxysmal arrhythmias, such as fibrillation and flutter, are seen more frequently in the aged, particularly in patients suffering from pneumonia and thyrotoxicosis.⁷⁰ When the rate is over 150, the presence of anginal pain with the arrhythmia is highly suggestive of the presence of coronary-artery disease.⁷¹ Persistent auricular fibrillation should arouse the suspicion of thyrotoxicosis. It is significant, however, that cases of persistent auricular fibrillation lasting as long as twenty-five years have been reported.⁷²

Blood pressure. Reported studies of the blood pressure present conflicting results. Some investigators found no change in average or modal blood pressure with increasing age.^{73, 74} Robinson and Brucer⁷⁴ excluded, however, all pressures of 140 systolic, 90 diastolic, and above. On the other hand, Master et al.,⁷⁵ in a series of nearly 15,000 men and women, found two thirds (males) to three fourths (females) of persons seventy years old and over to have blood pressures over 150 systolic, 90 diastolic. Other reports of smaller groups likewise contain a large percentage of persons in the older age group with systolic hypertension.^{76, 77} The systolic hypertension is probably compensatory for the loss of elasticity in the aging blood vessel walls. It is of some interest that the life expectancy of persons with systolic hypertension was of the same order as for those with normal blood pressure.⁷⁶ Thus it is probable that the presently accepted standards of normal blood pressure in the aged are too low. In nonhypertensive individuals, the diastolic blood pressure shows a tendency to fall with age,⁷⁶ with a resultant marked increase in pulse pressure. This is probably due to the rapid fall of pressure within the arteries during diastole,⁷⁸ for which compensation does not occur because of the diminished elasticity of the blood vessels.

Corrected erythrocytic sedimentation rate. The sedimentation rate is widely used in the diagnosis of myocardial infarction. It must be remembered, however, that there is a definite rise in the corrected erythrocytic sedimentation rate with age alone.⁷⁹ Values up to 0.7 mm. per minute by the Rourke-Ernstene method are apparently normal above the age of fifty, whereas in younger individuals the normal is 0.08 to 0.35 mm. per minute.

Electrocardiogram. The paucity of knowledge of the electrocardiographic changes consequent to age alone is reflected in the fact that most of the standard texts of electrocardiography have no listings for subjects as "aging," "aged" or "old age." Certain changes are known to occur, however, with sufficient frequency in the aged in the absence of other manifestations of cardiac disease to be

regarded as normal. Many of these same changes, nevertheless, are considered to be definite, although minor, abnormalities when they are found in younger subjects.

The most frequent of these changes in the electrocardiogram of the aged is a shift in the electrical axis of the heart to the left (or counterclockwise); this has been observed in well over 50 per cent of older patients.⁸⁰⁻⁸⁵ An associated but less frequent finding with the same significance is a prominent QS wave in Lead 3, and an inverted T₁. These changes probably derive from a more transverse position of the heart secondary to flattening of the diaphragm and perhaps also in part from a relative hypertrophy of the left ventricular mass with age in relation to the right ventricle. Thus, in a group of patients with marked left-axis deviation, Faulkner and Duncan⁸⁶ found normal-sized hearts by x-ray study in more than a third, whereas almost another third showed hearts that were anatomically normal.

Extrasystoles occur in about a third of elderly patients,⁸⁷ and as in younger groups, they constitute the usual electrocardiographic arrhythmia. Those of ventricular origin are about twice as common in occurrence as those of auricular origin. They assume pathological significance when frequent or when they show coupling or other rhythmic occurrence or multiple foci of origin.

With aging there is a slight increase in transmission time through the entire conduction system of the heart, reflected in a PR interval that frequently exceeds 0.20 second and an intraventricular interval that is often greater than 0.10 second.^{88, 89} Tendency to low voltage is found in all the component waves of the electrocardiogram.⁸⁵

There is less agreement concerning the frequency or significance of other isolated electrocardiographic findings in the aged; these include low or inverted T waves in leads other than Lead 3, deviation of ST segments, the duration of the QRS complex beyond 0.11 second, the presence of prominent Q waves in leads other than Lead 3, right-axis deviation, auricular fibrillation and marked bradycardia. Indeed, there is little agreement as to their significance in healthy young persons.⁸⁸

It is apparent from the above that there is no agreement among observers about the definition of the normal electrocardiogram for healthy old persons and about the frequency of occurrence of normal tracings in various age groups. Thus the incidence of abnormal electrocardiograms in groups of aged persons is cited by various authors as 0 per cent,⁸⁷ 26 per cent,⁸⁰ 41 per cent,⁸⁹ 67 per cent,⁸⁵ 85 per cent⁸² and 97 per cent.⁹⁰ Much of this discrepancy is accounted for by the inclusion in some series of old persons with definite clinical evidence of serious heart disease, such as cardiac enlargement, congestive failure or myocardial infarction,^{81, 91} and by great variability in the criteria of electro-

radiographic normality. The crux of the situation is that standards have not yet been established for older age groups. It appears, however, that over one-fourth of aged persons with no evidence of heart disease by careful history and physical examination show abnormalities in the electrocardiogram.^{50, 52, 53}

There are nowhere in the literature any reports of clinical, electrocardiographic and detailed pathological correlations in aged hearts, and it is therefore of some interest to cite certain preliminary observations in this regard.⁵¹ A survey was made of the records of hearts from 100 consecutive patients aged sixty-five and over studied at the Beth Israel Hospital by the injection-dissection technic of Schlesinger.⁵² In 29 cases the hearts showed coronary arteries essentially free of disease, and in 17 of these the heart could be regarded as clinically and pathologically normal. Ten of this group of patients with "normal" hearts were studied electrocardiographically. These patients did not differ in age or sex distribution from the entire group of 100. Five of these had entirely normal electrocardiograms, 2 had low T waves in Lead I, 2 had inverted T waves in Lead 4, and 1 showed the pattern of left-bundle-branch block. The last was the only patient in this group showing any increase in conduction time over the accepted standards for all ages; this is in contrast to the findings cited above. Left-axis deviation was present in 3 patients, right-axis deviation in 1, and in the remaining 6 the axis was normal. Three patients showed low voltage, and 2, ventricular premature beats. These observations, because of the small group involved, have no statistical significance. They illustrate, however, the type of study that will be necessary for the establishment in geriatric electrocardiography of standards that will separate disease and changed function due to normal aging.

To summarize, the following generalizations are thought to be of more significance than the few non-specific changes that may be found in the electrocardiograms of aging hearts. First, there is no electrocardiographic pattern of the senile or aging heart.⁵⁴ Second, the electrocardiogram even in the very aged may be identical in all respects with that of youth.⁵⁵ As in any age group, serious and far-advanced heart disease may exist without any reflection of its magnitude or even its presence in the electrocardiogram; this is especially true of coronary-artery disease.⁵⁴ Third, adequate clinicopathological and electrocardiographic correlations are needed in the aged as a basis for diagnostic and prognostic conclusions. Such studies might well be aided by a widespread use of electrocardiograms in the routine clinical examination of patients of middle age and beyond. Finally, it is evident from the foregoing that, even more in the aged than in young patients, the electrocardiogram must be viewed as a part of the total evaluation of the pa-

tient, which should include careful history-taking and physical examination and correlated laboratory studies. Nevertheless, the diagnosis of coronary sclerosis will be missed in a fair number of apparently healthy elderly persons.

X-ray studies. Certain minor changes have been described in the x-ray appearance of the heart and great vessels in the aged.⁵⁵ As the diaphragm becomes higher, the heart assumes a more horizontal position and the contour of the left ventricle becomes slightly more prominent. The aorta in its ascending portion increases in length and circumference and may show tortuosity. Dilatation may become so marked that the diagnosis of arteriosclerotic aneurysm must be made.⁷⁰ Cardiac pulsations do not have the vigor characteristic of earlier years. Calcification may be seen in the aorta and aortic knob, in the heart valves or valve rings or even in the coronary arteries; when present in the valve leaflets, it assumes clinical significance.

There is no agreement concerning the heart size and the changes that occur with aging, even with respect to pathological data, as the discussion above indicates. If such changes do occur constantly, it remains to be seen if they are of such magnitude as to be detectable by x-ray technics and standards for determining heart size. The more reliable of these standards are now based only on height and body weight.⁵⁶ For the present, therefore, significant or progressive increase in heart size by x-ray studies, even in the aged, should be interpreted as being generally indicative of heart disease.

TREATMENT

General considerations. As we have noted above, although there has been a large increase in the number of people living to the age of sixty-five or over, no increase in life expectancy for this group has been observed.

It should be stressed that the majority of persons in this age group have coronary-artery disease. Thus in the 100 cases that we studied,⁵¹ 63 patients had significant coronary-artery disease and the cause of death was cardiac in the majority. It is more striking that no clinical diagnosis of heart disease was made in 37 cases. In 15 of the latter cases the hearts showed extensive coronary-artery narrowing or occlusion, or both; in 1 case, that of a patient with lymphatic leukemia, a recently healed apical infarct was found. It is thus clear that although no clinical evidence of coronary-artery sclerosis may be present in a given patient, all elderly persons should be handled as if they had some degree of that disease. Progress would involve, therefore, among other things, preventive measures designed to prevent disturbances of function, congestive heart failure and acute cardiac accidents.

Surgery. The management of cardiac patients who require major surgery has been reviewed by

Blumgart.⁹⁷ Much of the discussion is pertinent to the older patient with no functional cardiac disturbance but with the statistical possibility of coronary-artery disease. The prevention of postoperative acute myocardial infarction depends on the avoidance of shock, which may follow hemorrhage, and severe infection. Hypoglycemia is of serious import in this regard in diabetic patients submitted to surgery. Hypotension associated with spinal anesthesia should be prevented by adequate use of sympathomimetic drugs having little effect on cardiac work, such as Paredrine or Neo-Synephrine. It should be stressed that rarely does an aged surgical patient die a primary cardiac death. Thus, Wilcox and Clagett⁹⁸ list 1204 patients over sixty-five years of age who underwent operations with a mortality of only 8 per cent for benign conditions and operable carcinoma. It was striking that only 20 per cent, however, failed to have a significant postoperative complication, such as thrombophlebitis, pneumonia, embolism, atelectasis or a cerebral or renal complication. Brooks,⁹⁹ however, points out that a third of a group of patients over seventy requiring abdominal section died in the hospital. Moreover, the survivors realized only a small fraction of their life expectancy. Wangenstein¹⁰⁰ stressed, on the other hand, the safety of multiple operations in patients adequately prepared with a preoperative period of high-protein, high-carbohydrate and low-fat feedings, adequate hydration and satisfactory electrolyte balance. It should be borne in mind, however, that edema may accumulate in a patient with poor cardiac reserve who is given a large amount of salt preoperatively or postoperatively, since approximately 1.0 gm. of salt retains 100 cc. of water.

Prevention of congestive failure. In last year's review¹⁰¹ certain forms of curable heart disease were discussed. It should be stressed that anemia and nutritional deficiency may have a deleterious effect on the normal heart, particularly in the aged. Dietary restriction is frequent in the aged because of the lowered metabolic requirements, changes in gastrointestinal function, depressed appetite, loss of teeth, lack of exercise and so forth. The recognition and adequate therapy of anemia and nutritional deficiency before cardiac complications such as angina pectoris and congestive heart failure have occurred are important. Tuohy¹⁰² has stated that the competence of healthy old people is largely a matter of nutrition. He emphasized the error in the idea that the elderly should be abstemious, while advocating a restriction of fat content in the diet of an inactive patient to 10 per cent of the necessary calories.

Burwell¹⁰³ summarized some of the factors tending to precipitate heart failure in patients with asymptomatic heart disease. The most important of these are infections, particularly respiratory infections, associated with fever, tachycardia and

cough, since they cause increased cardiac work and possibly a depression in cardiac efficiency. Bed rest, adequate chemotherapy and maintenance of oxygenation should minimize the injury to the heart.

Bed rest. Much has recently been written concerning the abuse of bed rest in elderly patients.¹⁰⁴⁻¹⁰⁷ It has been stated by Dock¹⁰⁴ that bed rest claims more lives than all other therapeutic agents added together. The evidence is, however, not conclusive, for many patients do poorly in the hospital because they are worn out by overvigorous investigation and overfrequent examination. The energy expended by a patient in a complete gastrointestinal roentgenologic study, for instance, is exhausting, particularly to an old person. Drastic changes in eating habits and in hours of sleep made necessary by hospital routine, together with the too frequent use of sedatives, may also act deleteriously in the aged. Particular emphasis has been placed on bed rest as a cause of occurrence of peripheral and pulmonary emboli.¹⁰⁴ Actually, however, the cause of thrombophlebitis is unknown, and it is perhaps as unscientific to ascribe the cause to bed rest as it is to say that bed rest has nothing whatever to do with its occurrence.

It is clear, nevertheless, that prolonged and absolute bed rest leads to muscular, possibly including cardiac, weakness and atrophy, in addition to pulmonary and other complications. The period of convalescence may therefore be unnecessarily prolonged. Good clinical judgment is thus of paramount importance in this matter.

Physical exertion. One has only to look at the obituary notices in newspapers to be impressed by the effect of severe physical exertion in elderly people. Boas¹⁰⁸ in particular has stressed the occurrence of acute myocardial infarction after severe physical or emotional stress. Aged patients should be warned to avoid such strain, particularly in the winter and also when they are fatigued.

On the other hand, an important and often neglected aspect of prolonging the useful lives of the aged is making living worth while for them. Too often they live in an insulated atmosphere that promotes physical and mental atrophy because of an imposed isolation. Psychometric studies actually demonstrate a wide range of individual variations in the aged in intellectual ability, physical skill and interests.¹⁰⁹ The family physician can play an important role in helping to devise a program of activities for his elderly patients that is adapted to these individual variations in mental and physical capacities.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 30481

PRESENTATION OF CASE

A fifty-seven-year-old housewife entered the hospital because of intermittent sharp pain in the lower abdomen.

The patient was perfectly well until one month before entry, when she was troubled by mild lower abdominal "cramps" of several days' duration. Her bowels remained regular, however, with at least one bowel movement a day. She noted that there was a fair amount of mucus passed with the stools. Two weeks before entry she began to have sharp colicky pains, which started in the right lower quadrant and passed across to the left lower quadrant. These caused her to double up in agony, but no nausea or vomiting was present. The pains lasted throughout the day, and with each attack she had the urge to move her bowels, though nothing was passed by rectum. Her doctor made a diagnosis of "abdominal stasis" and gave her a cathartic. This resulted in a copious bowel movement and complete relief. She continued to eat heartily and to have a daily bowel movement until one week before entry, when her bowels did not move for a day and she took a cathartic. The next day she again had an attack of lower abdominal pain similar to that of the first attack. She took several doses of milk of magnesia, which made the pain worse. Nausea and vomiting set in, and she vomited green-colored mucus. Five days before entry she had a normal bowel movement, with relief from pain. She still felt poorly, however, and had lost her appetite. Several enemas were poorly retained and brought little return. Four days before entry her doctor felt a tender "bunch" in the left lower quadrant and advocated hospitalization. She had

had no further recurrences of pain and had had daily bowel movement. No blood had been noted in the stools. She had lost an estimated 20 pounds in weight in the month before entry.

She had had a right oöphorectomy and salpingectomy for "cyst" many years before admission followed by removal of the other internal organs some years later.

Physical examination showed a well-developed, rather obese woman in no apparent distress. The heart and lungs were normal. The abdomen was negative. Peristalsis was normal. There was slight tenderness in the left lower quadrant to deep palpation during pelvic examination. A firm, reddish, pedunculated mass, the size of a small pea, protruded from the depression in the apex of the vagina. Rectal examination revealed a walnut-sized, irregular, smooth, hard, painless mass on the anterior rectal wall about 10 cm. above the sphincter.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 100°F., the pulse 84, and the respirations 28.

Examination of the blood showed a white-cell count of 10,000, with 90 per cent hemoglobin. The urine was acid, with a specific gravity of 1.024; it gave a + test for albumin and there were 8 red cells per high-power field in the sediment. A Hinton test was negative. The blood chemical findings were normal. X-ray films of the chest and intravenous pyelograms were negative. A barium enema showed passage of the barium through the rectosigmoid junction to the lower sigmoid, at which point there was a narrowed portion of intestine through which a thin stream of barium passed. There was a suggestion of a shelf deformity, but no evidence of ulceration (Fig. 1). Proctoscopic examination revealed normal rectal mucosa up to 13 cm., where an extraluminal obstruction was found encroaching anteriorly. The proctoscope could not be passed beyond this lesion. The mucosa immediately beneath was granular and hyperemic but intact.

On the fifth hospital day the patient developed diarrhea and a fever of 101°F. Examination at that time was essentially as before. She was given 5 gm. of sulfasuccidine three times daily, and on the tenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. OLIVER COPE: This patient had intestinal obstruction of one month's duration. The point of

*On leave of absence.

struction was the pelvic portion of the large rel.

We are given no detailed information regarding previous pelvic operations. I take it that these operations were not performed in this hospital and it we have neither a surgical nor a pathological report. Knowledge of the previous pelvic disease might make a difference. It might be related to the anatomic abnormality reported in the vaginal examination, or the latter may be a red herring thrown across our path, it and the previous pelvic disease having nothing to do with the present complaint. In the physical examination, the uterine cervix is not mentioned. One must therefore assume that the

effort to reduce the growth of organisms and, therefore, the volume of feces in the colon. Presumably the operation was for relief of the obstruction.

In order to arrive at a diagnosis it is necessary to consider all those lesions that can produce obstruction in the sigmoid. The x-ray studies as reported tend to exclude primary carcinoma of the sigmoid. Since the x-ray examination is extremely important, I shall ask Dr. Schulz if he has anything to add to the report. I trust that he will comment on the absence of ulceration and on the nature of the constriction.

DR. MILFORD SCHULZ: There is an area of narrowing in the sigmoid. I do not see the shelf that was



FIGURE 1 Roentgenogram Following Barium Enema
Arrows indicate area of narrowing in sigmoid.

hysterectomy had been a total one. If this is true, the mass palpated on the anterior rectal wall did not represent the cervix but an abnormal mass.

The negative intravenous pyelogram is important. We may assume in the first place that the disease is not primary in the urinary tract and, secondly, that the lesion in the pelvis did not affect either the ureter or the bladder. Had the hysterectomy been one for carcinoma of the cervix and had the mass been a recurrence of the carcinoma in the pelvis, one might well have expected the mass to have been more to one side or the other and to have produced obstruction of one of the ureters, with hydronephrosis.

It is obvious that the physician in charge made a diagnosis of incomplete obstruction. The patient was carried for ten days on sulfasuccidine in an

effort to reduce the growth of organisms and, therefore, the volume of feces in the colon. Presumably the operation was for relief of the obstruction.

DR. COPE: Enough barium got by the loop for a satisfactory examination?

DR. SCHULZ: Yes; the bowel proximal to the narrowing is not widely dilated, and the obstruction is not complete. No diverticulums are evident.

DR. COPE: The fact that no diverticulums were visualized does not in itself exclude diverticulitis, but if the obstruction in this patient was due to diverticulitis, I should have expected a more extensive involvement of the bowel than what is present. The involved area is limited, the upper sigmoid not being involved.

DR. SCHULZ: The proctoscopic examination describes the lesion in the rectosigmoid. The lesion demonstrated here is higher up.

DR. COPE: Is there any evidence by x-ray of an extrinsic mass? I do not want to pin you down too far. Do I understand that you would not ascribe the lesion to carcinoma because of the absence of ulceration, or to diverticulitis because of the lack of involvement of the other part of the bowel?

DR. SCHULZ: I do not believe that one can rule out carcinoma, especially in view of the questionable shelf that was described. Certainly its appearance is not characteristic.

DR. COPE: From both the physical and x-ray examinations the abnormal mass was small and the area of the bowel involved was short. A malignant lesion is a better explanation than an abscess. I am not sure, however, whether the mass was intrinsic or extrinsic in relation to the sigmoid. Thus far I favor a diagnosis of primary cancer of the sigmoid, but I cannot exclude either diverticulitis of the sigmoid or an extrinsic lesion causing obstruction of the sigmoid.

In the latter category three conditions should be discussed. In the first place, endometriosis of the pelvic peritoneum can involve the sigmoid in such a way as to cause obstruction. This would be unusual in a woman past the menopause, for in the absence of continued ovarian activity the endometrial-like tissue should undergo atrophy. There are, however, endocrine sources other than the ovary for estrin-like hormones, such as the adrenal cortex. In the second place, one should consider gravitational metastases with involvement of the sigmoid. The primary lesion for such a carcinoma might be the stomach or some other organ in the upper abdomen. And, third, I should like to mention, for I have seen it once, adenoacanthoma arising in the cervix and later involving the large bowel. In 1931, I operated on a woman for what appeared to be a primary malignant tumor of the large intestine producing obstruction. Two years previously she had had an adenoacanthoma of the cervix excised surgically. At my operation an adenoacanthoma of the large bowel, presumably a metastasis from the primary lesion, was disclosed. In the absence of knowledge regarding the previous pelvic lesion, one cannot afford to make such a diagnosis. I am left with the only tenable diagnosis, that of a primary malignant tumor of the lower sigmoid.

DR. LELAND S. McKITTRICK: Some years ago I resected a sigmoid for a woman in her early sixties; the lesion, which we had interpreted as a carcinoma, proved to be an endometriosis. There was no other evidence of ovarian activity. She had the menopause in the usual way — over a long period of years. Is there any less likelihood of endometriosis in a person with a surgical menopause than in one who has had a normal one?

DR. COPE: I should think that there was. In producing the surgical menopause, the operator would presumably have removed in his operation the majority of endometrial implants. Less tissue would have remained to contract and to produce bowel obstruction.

Was there active tumor proliferation or only scarring in your case?

DR. McKITTRICK: There was real tumor formation. I cannot give the details of the microscopical findings, but it was more than just scarring.

DR. COPE: As I have said, there are the other endocrine sources for continued mild stimulation of the endometrium, such as the adrenal cortex.

DR. ANNE FORBES: Are you sure that no one gave this patient estrin?

DR. COPE: That is a good point. Estrin therapy after the menopause would have reactivated endometrial tissue. If this patient had received estrin in large doses, she might have developed a pelvic endometrial tumor.

DR. FRANCIS D. MOORE: So far as we know the patient had not received estrin therapy. The pelvic operation was done many years before entry. The mass in the apex of the vagina was just a mucosal tab.

DR. COPE: The tab was a red herring.

DR. MOORE: Our line of reasoning was similar to that of Dr. Cope. The mass felt by rectum and seen by proctoscopy was caused by extrinsic pressure of a neighboring loop. We thought preoperatively that it was in all likelihood a carcinoma of the sigmoid. At operation we did not find anything to change our opinion. The pelvis was surprisingly free — no mass and no extensive inflammatory or neoplastic disease. There was a small sclerosing lesion that had every appearance of an annular carcinoma of the sigmoid. A combined abdominoperineal resection was done after freeing it. After removal, the bowel was opened, and looking at it grossly, we still thought that we were dealing with a carcinoma of the sigmoid.

CLINICAL DIAGNOSIS

Carcinoma of sigmoid.

DR. COPE'S DIAGNOSIS

Carcinoma of sigmoid.

ANATOMICAL DIAGNOSIS

Diverticulitis of sigmoid.

PATHOLOGICAL DISCUSSION

DR. RONALD C. SNIFFEN: Dr. Moore removed about 48 cm. of rectum and sigmoid. The rectum was normal. Above the peritoneal reflection there was an 18-cm. segment of sigmoid, which looped down anteriorly to fix itself against the anterior portion of the sigmoid near the point of the peri-

fecal reflection. Here, there was a mass of adhesions, which apparently formed the tumor that was seen. Throughout the sigmoid there were many diverticula, and we found that sinus tracts ran to the mass from both the distal and proximal portions of the sigmoid loops. The mass consisted of chronic inflammatory tissue and was undoubtedly due to diverticulitis. At the point where the proximal portion of the sigmoid was fixed to the inflammatory mass there was an appreciable narrowing of the lumen.

DR. COPE: Dr. McKittrick, how often do you see sharply localized diverticulitis that is difficult to distinguish from carcinoma at operation?

DR. MCKITTRICK: I do not know, but I can tell you that I have just sent a patient home for whom at the end of operation I gave the family a poor prognosis because I thought that he had incurable carcinoma. I did not open the specimen and was overwhelmed when the report was diverticulitis. I see it infrequently enough so that I was badly misled, but frequently enough so that it is not a rarity.

DR. COPE: The X-ray Department does better than we do. Dr. Schulz, if I am correct, was against cancer because of the appearance of the mucosa.

DR. MCKITTRICK: On the other side of the ledger is the fact that we not infrequently discover an abscess from a diverticulitis when the radiologist has found nothing.

DR. SCHULZ: We do not see a diverticulum unless it is filled with barium. In this case, the diverticula did not fill. An intact mucosa is helpful, if you can be sure of it, and likewise, a good shelf.

CASE 30482

PRESENTATION OF CASE

A fifty-eight-year-old single nurse entered the hospital for study.

For fifteen years the patient had had intermittent sensations of fullness in the right upper quadrant of the abdomen and vague distress after meals. Nine years before admission a gastrointestinal series was negative. One year later she started to have intermittent gross melena attributed to hemorrhoids. This condition persisted. About one year before entry the distress in the right upper quadrant became severer. There were definite jaundice, light-colored stools and dark urine for one week, at the end of which time a cholecystectomy and cholecystostomy were performed at a hospital in another city. Postoperatively she had a stormy course, with increasing jaundice and clay-colored stools, which eventually, however, cleared up. She apparently remained well, except for occasional bouts of epistemic distress, until ten weeks before entry when she developed pruritus, followed four weeks later by frank jaundice, increasing light-colored stools

and dark-colored urine. One week before entry she was admitted to a community hospital where she was treated medically, with amelioration of the symptoms. Since the jaundice persisted, she was transferred to this hospital. She had lost 30 pounds in weight in eleven months. The only vomiting she had had was induced, and she thought that it relieved the distress in the right upper quadrant. She had had no chills or fever.

Physical examination showed a thin, deeply jaundiced woman. The lungs were clear. The heart was normal in size. The liver edge was palpable three fingerbreadths below the costal margin. Slight tenderness was elicited in the right upper quadrant, but no masses were palpable.

The blood pressure was 144 systolic, 82 diastolic. The temperature was 99°F., the pulse 76, and the respirations 20.

Examination of the blood showed a white-cell count of 5700, with 71 per cent neutrophils and 18 per cent lymphocytes; the hemoglobin was 8.5 gm. per 100 cc. The urine was normal. A blood Hinton test was negative. The stools were reddish-brown and gave a ++++ guaiac test. The serum protein was 6.2 gm. per 100 cc. The serum bilirubin was 6.65 mg. per 100 cc. direct, and 8.8 mg. indirect.

Plain films of the abdomen and chest were negative. A barium enema showed normal filling of the rectum and rectosigmoid. Just beyond the rectosigmoid junction there was a constant area of narrowing that appeared to be due to a filling defect on the superior wall of the sigmoid measuring about 4 cm. in length. On one film a shelf could be seen at the distal end of this defect. The remainder of the colon showed no abnormality. The transverse colon dipped down into the pelvis to overlay the abnormal area, which was therefore not visible in the subsequent films. Post-evacuation films showed only moderate contraction of the colon and a large amount of fecal material was still visible in it; the sigmoid was obscured by the transverse colon. In all the films the upper abdomen was unusually dense, but no soft-tissue outline was demonstrable. Re-examination of the colon after the introduction of air showed numerous small rounded areas of diminished density that may have been due to fecal material intermingled with the barium.

The patient was given several transfusions, and on the fifteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: We have a patient fifty-eight years of age whose symptoms began fifteen years before entry, with fullness and distress in the right upper quadrant after meals. Nine years before entry a gastrointestinal series was done, and I presume that it was negative. The examination was probably limited to the stomach and small bowel since nothing is said about the colon. It would

be interesting to know whether she had had a barium enema at that time. The statement "One year later she started to have intermittent gross melena attributed to hemorrhoids" needs a little comment. I do not believe that one ever ought to attribute bleeding from the rectum to hemorrhoids until all other possibilities have been ruled out. It is extremely dangerous in a patient with hemorrhoids to say that the bleeding is coming only from hemorrhoids without a complete rectal and sigmoidoscopic examination, since it may be coming from a lesion higher up in the colon that is often overlooked until it becomes inoperable. One year before admission the distress in the right upper quadrant became severer and associated with it were jaundice, clay-colored stools and dark urine. At that time a cholecystectomy and choledochostomy were done at an outside hospital. The postoperative course following these operations does not seem just right for cholecystitis and cholelithiasis, in that it states that she had a stormy convalescence with increasing jaundice and with clay-colored stools, which eventually cleared up. Ordinarily when one operates on the gall bladder and drains the common duct, as I presume was done in this case, a tube is sutured into the common duct so that the patient's bile can drain externally rather than into the duodenum. If the patient were treated in this manner and if the jaundice was purely obstructive, it is surprising that she developed increasing jaundice. It is possible, of course, if the jaundice was due to intrahepatic disease, that the operation produced additional liver injury, thus causing the jaundice to become more pronounced.

DR. FRANCIS D. MOORE: I can clear up that point. She did have a tube put in, and it was after it was taken out that the jaundice appeared.

DR. LINTON: That is an important fact to know, because it probably means there was some obstruction in the distal part of the common duct, either postoperative stricture, inflammation, stone or malignant growth, that was temporarily occluding the outlet of the common duct.

The patient was apparently well for most of the following year. Ten weeks before entry to this hospital, however, she developed pruritus, and six weeks before admission, she again had jaundice, with light-colored stools and dark urine. It is interesting to note that in the previous year she had lost 30 pounds and that she had had no chills or fever. If she had had a common-duct stone I think that she probably would have had an associated cholangitis, with chills and fever. Nothing is said about pain, so that we have no clue whether or not she had a stone, provided that we base the diagnosis of cholelithiasis on colicky pain in the right upper quadrant.

To go on with the physical examination, the only thing that is to be noted is that she was jaundiced and had an enlarged liver. We have nothing else

to help in the diagnosis. The hemoglobin was low, 8.5 gm., which is probably of significance. There is one statement regarding the urine that I do not believe is correct, "The urine was normal." I cannot conceive of a patient having a serum bilirubin of 15 mg. without some bile in the urine. It is possible that she had hemolytic jaundice, in which one does not see bile in the urine, but I doubt it.

I should also like to know whether a rectal examination and a proctoscopic examination were done. From a clinical point of view I cannot come to a conclusion without those examinations, especially in view of what the x-ray film of the colon showed.

DR. MOORE: Both were done. The rectal examination was negative, except for the fact that definitely gross blood was present. Proctoscopy was negative except for gross blood coming from above.

DR. LINTON: Have we the x-ray films? I do not know whether to look at them or not; they usually confuse me.

DR. LAURENCE L. ROBBINS: These are confusing; to say the least. I had considerable difficulty finding any films that demonstrated the lesion. So far as I can determine it is hidden in these loops of sigmoid, but on this spot film one can follow the rectum up to what is apparently the beginning of the sigmoid. Here one can see a definite shelf-like margin. On this spot film one can also see a shelf and what appears to be an area of ulceration in the center of the lesion. There is no evidence of polyposis.

DR. LINTON: I am really confused now. I had considered polyposis as a possibility because of the bleeding from the rectum. In view of the fact that neither proctoscopy nor the x-ray examination showed polyps, I must rule it out.

It seems to me that we have a patient who presented two conditions. I do not like to diagnose two conditions, and I should like to reason it out so that I can make one final diagnosis to explain the facts. This woman had obstructive jaundice and an ulcerating lesion in the rectosigmoid. I should like to know if a gastrointestinal series was done.

DR. BENJAMIN CASTLEMAN: It had been done at another hospital before she came here, and was said to be negative.

DR. LINTON: First of all, what conditions can produce jaundice in a patient who has had a cholecystectomy and a choledochostomy?

The first thing that enters my mind is the question whether she had developed stricture of the common duct secondary to the operation. That diagnosis, I believe, is a little unlikely because she was well for an interval of a year after the operation and seemed to have no evidence of jaundice during that period. It is unusual for a stricture to manifest itself a year after operation. If a patient has had damage done to the common duct, jaundice generally develops immediately or in a matter of a

weeks or months and persists rather than lets as happened in this patient. So I believe that can rule out stricture of the common duct as a cause of the recurrent jaundice.

Another possibility that one has to consider is carcinoma of the common bile duct. I believe that the history was too long for carcinoma of the bile duct. Malignant disease of the common duct usually obstructs the common duct early, and jaundice becomes pronounced in a short time — a matter of weeks.

Another possibility is carcinoma in the region of the ampulla, but I know of no way to be sure of such a diagnosis. I do not know whether one can pick up gallstones with a carcinoma in the region of the ampulla in the way that one can with a carcinoma of the gall bladder, which is practically always associated with gallstones. The fact that this patient had gallstones, and I presume that she had, makes me think that carcinoma in the region of the ampulla of Vater is a definite possibility. How are we going to explain such a diagnosis with the x-ray findings of a lesion in the rectosigmoid that is apparently malignant? Is that a justifiable conclusion?

DR. ROBBINS: Yes.

DR. LINTON: I am disturbed by the fact that the lesion was not seen on proctoscopic examination. Barium enemas of the rectosigmoid are not always accurate; but I should think that if the proctoscope had been passed its full length this lesion would have been visualized.

DR. CASTLEMAN: The first proctoscopic examination at the other hospital was unsatisfactory because there was too much fecal material. After she had been cleaned out, sigmoidoscopic examination was possible for only about 18 cm., where a right angle was encountered.

DR. MOORE: She was proctoscoped again here with the same unsatisfactory results.

DR. LINTON: Another possibility to explain the rectosigmoid lesion is a peritoneal implant from a carcinoma elsewhere in the intestinal tract that had deposited itself in the pelvis and had secondarily involved the rectosigmoid.

Another possibility that would explain the jaundice is carcinoma of the rectosigmoid with metastases to the liver. The patient had an enlarged liver, but the physical examination does not state whether it was nodular. I should expect it to have been nodular if it was so full of metastases to produce obstructive jaundice. Also, if it was due to metastatic disease, the metastases would have to be so local that they obstructed the common duct rather than the biliary radicals of the liver. I believe that is true because one can tie off 90 per cent of an animal's biliary system without its becoming jaundiced. It seems to me that, with the additional help from these statements about proctoscopy and

the barium enema, one cannot rule out the diagnosis of carcinoma of the rectosigmoid. I should be a little happier, however, if it had been felt by rectal examination or had been seen by proctoscopy. The only way that I can possibly connect the jaundice with such a lesion is to assume that metastases had localized around the common duct sufficiently to produce obstruction. I am therefore going to make a diagnosis of carcinoma of the rectosigmoid, with metastases to the liver in the region of the common duct and with obstruction of the latter.

DR. JOSEPH C. AUB: Does not the x-ray film show a colossal liver shadow pushing down the colon and shoving the stomach to one side?

DR. ROBBINS: I cannot be sure, but I doubt it.

DR. AUB: Does it not also show a big spleen?

DR. ROBBINS: There is slight enlargement of the spleen.

A PHYSICIAN: How does Dr. Linton explain the rectal bleeding eight years before entry?

DR. LINTON: I think that we have to explain it on the lesion in the rectosigmoid. It is possible to have a slowly growing lesion, although it is a little unusual.

DR. CASTLEMAN: If she had carcinoma, one can presuppose that it started as a polyp and later became malignant; of course, she also may have had hemorrhoids.

DR. AUB: If she had jaundice due to a neoplasm that disappeared and recurred, one has to assume that there was necrosis of the neoplasm, which relieved the tension and allowed bile to drain.

DR. CASTLEMAN: That happens with intraductal lesions but not with those exerting extrinsic pressure. For example, a tumor of the papilla of Vater often produces intermittent jaundice.

DR. MOORE: Dr. L. S. McKittrick operated on this patient, and his reasoning was much like that of Dr. Linton except that he thought the fact that the jaundice came and went was definite evidence against a neoplastic lesion in or about the common bile duct. Even taking into consideration the mechanism that Dr. Aub mentioned, it would still seem to be nonmalignant if it was capable of fluctuating.

CLINICAL DIAGNOSES

Stricture of common duct?

Carcinoma of sigmoid.

DR. LINTON'S DIAGNOSES

Carcinoma of sigmoid, with metastases to liver in region of common bile duct.

Obstructive jaundice.

ANATOMICAL DIAGNOSES

Stricture of common bile duct, traumatic, with biliary fistula.

Obstructive jaundice.

Adenocarcinoma of sigmoid.

PATHOLOGICAL DISCUSSION

DR. MOORE: At operation this patient was found to have had previous injury to the common duct that had completely destroyed 2 cm. of the duct. She had spontaneously formed a fistula in the scar tissue between the severed ends of the duct that let bile into the duodenum from time to time; the liver was enlarged because of the prolonged biliary obstruction but there was little evidence of biliary cirrhosis. In the midsigmoid was a sclerosing carcinoma.

DR. CASTLEMAN: At the first operation Dr. McKittrick repaired the common bile duct, using a vitallium tube, and at the second operation two weeks later, he resected the sigmoid and found what proved to be a slowly growing adenocarcinoma without metastasis to the regional nodes. The lesion itself was about 4 cm. in diameter and involved about half the circumference of the bowel.

It is surprising that the radiologists, both here and at the other hospital, had a difficult time finding the lesion in the sigmoid.

DR. ROBBINS: That is not hard to understand. In a markedly redundant sigmoid it is difficult to bring each loop into profile so that it can be seen in the fluoroscope. This is one of those cases, and it is surprising that the lesion was recognized at all.

DR. MOORE: The liver was not so big as it appeared in one of the x-ray films. It is deceiving, I suppose, because of the angle at which the film was taken.

DR. CASTLEMAN: Biopsy of the liver showed little parenchymal disease.

DR. LINTON: I still think it is rather unusual for a traumatic stricture of the common duct to manifest itself in this way.

DR. MOORE: It was not the usual type of traumatic stricture. A portion of the duct had been injured or destroyed at the previous operation. We were amazed that there was any bile in the duodenum. When we opened it and a probe was passed into the papilla, it proceeded 2 or 3 cm. and then came to a dead end. The duct was opened at that point, and 2 cm. was found to be missing before the hepatic duct was reached.

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THE ORGANIZATION OF MEDICAL CARE

PHYSICIANS will do well to consider carefully the two papers appearing elsewhere in this issue of the *Journal* that deal with the place of the physician in the modern world. Dr. Kretschmer presents the orthodox views of those whose ideas have dominated organized medicine in this country; namely, that the marvelous achievements of American medicine spring from the freedom allowed the individual physician and that any fundamental change in the present system of medical practice will lead to regimentation and consequent stagnation. This point of view has been widely publicized through the editorial columns of the *Journal of the American Medical Association* and the literature distributed

by the National Physicians' Committee. The essence of the argument of this group is that the organization of medical care is the concern of the medical profession alone. Most physicians are familiar with the argument, and many agree with it. Nevertheless, there are other points of view, both within the profession and among the hundred and thirty million Americans who, as patients, have a very direct interest in both the quality and the cost of medical care. In considering any problem, it is always well to view it in historical perspective, and for doctors particularly it may be worth while to examine objectively the place of their profession as it appears to a member of another profession — the law — that attempts to train its practitioners to take a broad and dispassionate view of human society. For these reasons, the paper by Mr. Berge should be read and pondered — but not necessarily agreed with — before anyone arrays himself in the ranks of those who champion the rights of the individual physician as the sole arbiter of systems of medical practice.

Certain facts appear to be inescapable. First, the cost of medical care, including payment for professional service, drugs and hospitalization, constitutes a considerable portion of our national expenses; second, the costs of illness, striking the individual unexpectedly, frequently exceed his capacity to pay at that particular time; third, it is possible to insure against such risks; and, finally, more and more people are beginning to consider good medical and hospital care and adequate health protection as essential. There can be little dispute about these facts; even the National Physicians' Committee has come to the conclusion that the public wants prepaid medical care, and Dr. Kretschmer states that the medical profession "is keenly aware of the importance of increasing the distribution of good medical service to all the people."

The dispute rages not so much over what is needed as on how to achieve it. Many plans are in the air, ranging from the far-reaching provisions of the Wagner-Murray-Dingell Bill in this country and the plan for a national health service as outlined by the White Paper¹ in Britain to individual agreements between physicians and their patients to provide professional service on an annual-payment

basis. Massachusetts has been one of the states in which there has been a lot of interest in finding a way to solve the problem of the distribution of medical care more equitably both for the patient and for the doctor. The White Cross Plan, sponsored as an experiment along these lines, aroused a great deal of comment, and subsequently the Massachusetts Medical Society launched the Blue Shield Plan. It is to be hoped that the latter, which admittedly gives only partial coverage at present, will continue to evolve until far more adequate service is provided.

Basically, there are two problems with which both the public and the medical and allied professions are concerned: that of paying for medical care and that of assuring the highest quality of medical care for the most people. The first is purely an economic problem, and almost any solution is bound to benefit both the public, which bears the costs, and the physicians, nurses, hospitals and other non-tax-supported groups that provide medical service, much of it on a partial or complete charity basis. The second problem has economic, political and technologic aspects. Its technologic phase is obviously the sole concern of the medical profession, which alone has the knowledge on which to base judgments of the quality of professional service or to institute improvements in the care of patients, in institutional standards or in the training of physicians. The public, however, has a direct concern in seeing to it that advances in medicine are made available as rapidly and as widely as possible. Here is the chief source of friction, since, in order to achieve the double objective of distributing the costs of medical care most equitably and of providing the best quality of medical service to the largest number of persons, governmental intervention at either the local or the federal level is contemplated. One group believes, with some justification, that the quality of medical service available to the country as a whole is inadequate compared with what it ought to be, both as regards hospital and laboratory facilities and the professional competence of those who utilize them. The other group contends, also with some justification, that facilities may not be ideal but are adequate in most portions of the United States, that these are being constantly

improved by organized medicine and that any advantage gained temporarily in the improvement of professional standards made possible by a federal scheme would soon be lost in the inevitable political regimentation that would result.

These are matters with which every physician should be concerned both as a citizen and as a doctor. The inertia of the bulk of the profession, combined with an opposition to change on the part of medical organizations, has led to a situation in which public opinion has forced the hand of the medical profession. Now the inevitability of some change is generally accepted. It is to be hoped that more local experimentation with different plans will be possible before a national health program is organized, so that the latter can be based on knowledge gained through experience. Those who wish to keep themselves informed on developments in this field should follow the reports published in the "Organization Section" of the *Journal of the American Medical Association* and should read the British White Paper, the text of the Murray-Wagner-Dingell Bill and a report to be published² that summarizes the ideas of those who have been particularly concerned with the development of a national health program. This is a field that should be approached with the same objectivity and detachment as a scientific experiment, so that the profession may make real contributions toward the solution of a problem with which both physicians and the general public are deeply concerned.

REFERENCES

1. *A National Health Service*. A statement by the Ministry of Health and the Department of Health for Scotland. 85 pp. New York: The Macmillan Company, 1944.
2. *Principles of a Nation-Wide Health Program*. A report of the Health Program Conference. 36 pp. New York: Committee on Research in Medical Economics, 1944.

MASSACHUSETTS MEDICAL SOCIETY COMMITTEE ON MEDICAL INFORMATION BUREAU

The appended statement has recently been forwarded to the secretaries of all district medical societies of the Massachusetts Medical Society, as well as to various hospitals.

WALTER G. PHIPPEN, *Chairman*
* * *

The Massachusetts Medical Society has established the Bureau of Clinical Information at its headquarters, 8 Fenway, Boston, as a means of augmenting its postgraduate educational effort.

The Bureau will supply information concerning the daily activities of the approved hospitals in Boston and its immediate vicinity. This information will deal with each hospital's daily schedule of operations, medical and surgical rounds and clinics, including the names of those pre-acting over these various activities and the location of the clinics. From time to time the Bureau will make available a bulletin that will list the fixed medical meetings and conferences held in the metropolitan area. This will be sent to hospitals, medical schools and physicians on request, and will be available at the Bureau. In brief, the ultimate aim of the Bureau is to serve the profession as a clearinghouse for all sorts of medical information.

The Bureau will be open from 7:00 a.m. to 10:00 a.m. and from 3:00 p.m. to 8:00 p.m., except Saturday afternoons. Information will be given by telephone.

You are requested to acquaint the physicians of your area with this new activity. No expense is involved on the part of those using this service.

ARTHUR W. ALLEN, M.D.

MICHAEL A. TIGHE, M.D.

WALTER G. PHIPPEN, M.D., *Chairman*

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CHANGES IN ISOLATION AND QUARANTINE REQUIREMENTS

A new printing of the isolation and quarantine requirements of the Massachusetts Department of Public Health, embodying recent changes, is now ready for distribution. Copies may be obtained by writing to the department.

Since the last revision, in 1941, three additional diseases (chancroid, granuloma inguinale and lymphogranuloma venereum) have been added to the reportable list and several changes in the previous regulations have been made. The major changes are as follows:

REGULATIONS

Chancroid. Column 1, placed in table immediately after "Asiatic cholera." Column 2, "No restrictions if under continuous treatment." Column 3, "No restrictions if examination demonstrates absence of infection." Columns 4 and 5, "Same as for adults." Column 6, "No."

German measles. Column 2, amended to read, "Three days from appearance of rash."

Gonorrhea. Column 2, omitted "See 'Regulations Governing the Control of Gonorrhea and Syphilis'" and substituted "No restrictions if under continuous treatment." Column 3, "No restrictions if examination demonstrates absence of infection." Columns 4 and 5, "Same as for adults." Column 6, "No."

Granuloma inguinale. Column 1, placed in table immediately after "Gonorrhea." Column 2, "No restrictions if under continuous treatment." Column 3, "No restrictions if examination demonstrates absence of infection." Columns 4 and 5, "Same as for adults." Column 6, "No."

Lymphogranuloma venereum. Column 1, placed in table immediately after "Lymphocytic choriomeningitis." Column 2, "No restrictions if under continuous treatment." Column 3, "No restrictions if examination demonstrates absence of infection." Columns 4 and 5, "Same as for adults." Column 6, "No."

Measles. Column 3, omitted "Note 1" and substituted "No restrictions." Column 5, amended to read "No restrictions."

Meningitis, meningococcal. Column 2, amended to read, "Two weeks from onset of disease (five days in cases adequately treated with sulfonamide drugs), and thereafter until all acute symptoms have subsided."

Meningitis, other forms, such as Pfeiffer bacillus, pneumococcal, streptococcal, etc. Column 1, order of words changed

to read "Meningitis: Pfeiffer bacillus, pneumococcal, streptococcal and other forms."

Scarlet fever. Column 2, amended to read: "Uncomplicated cases: Adults, two weeks; children, three weeks from date of appearance of rash. Examine nose, throat and ears to detect existence of discharge or inflammation before considering case as uncomplicated. (If upper respiratory tract symptoms appear during month after release from isolation, re-establish precautions.) Complicated cases: Four weeks and thereafter until abnormal discharge shall have ceased, swollen glands subsided or three successive cultures of abnormal discharge shall have been found free of hemolytic streptococci." Column 3, amended to read, "No restrictions except for milk handlers and schoolteachers who may continue their occupation only with special permission of the local board of health." Column 5, amended to read: "Until child lives away from home one week; no restrictions thereafter, if child continues to live away from home. Quarantined contacts living in a household with a case should be allowed to return to school at the same time as the patient is released from isolation."

Syphilis. Column 2, omitted "See 'Regulations Governing the Control of Gonorrhea and Syphilis'" and substituted "No restrictions if under continuous treatment, except as given in Note 5." Column 3, "No restrictions if examination demonstrates absence of infection." Columns 4 and 5, "Same as for adults." Column 6, "No."

Whooping cough. Column 3, omitted "Note 1" and substituted "No restrictions."

NOTES

Note 1. Incorporated in new Note 2. New Note 1 reads, "Definition of adult: Any person who has reached his eighteenth birthday is considered to be an adult for purposes of these regulations."

Note 2. Now includes old Note 1.

Note 4. Omitted entirely; substituted Note 5, renumbered.

Note 5. Changed to Note 4; substituted "Patients who have lesions of primary or secondary syphilis on exposed parts of the body or in the mouth, and are employed in any occupation requiring regular, direct contact with other persons, such as barber, hairdresser, manicurist, waiter, waitress, nursemaid, domestic, etc., shall be reported by name, address and occupation to the State Department of Public Health, unless the physician will assume responsibility for seeing that the patient discontinues such occupation until the lesions are healed."

Note 8. Omitted entirely; substituted "All of the above diseases except five should be reported to the local board of health. The five exceptions (chancroid, gonorrhea, granuloma inguinale, lymphogranuloma venereum and syphilis) should be reported directly to the State Department of Public Health on special forms, provided upon request."

IMMUNE SERUM GLOBULIN FOR MEASLES

For the past two and a half years the Division of Biologic Laboratories of the Department of Public Health has been collaborating with the Department of Physical Chemistry of the Harvard Medical School (under contract with the Office of Scientific Research and Development), the American Red Cross, the Bureau of Medicine and Surgery of the United States Navy and associated clinical and other groups in the development and use of a purified antibody fraction from human plasma. This study followed the successful purification of human serum albumin by a process developed under the same sponsorship and collaborative efforts. A number of physicians in Massachusetts have become familiar with this antibody fraction, known officially as "Immune Serum Globulin" (but known to many by the chemist's name "gamma globulin") through the preparations distributed to them from

basis. Massachusetts has been one of the states in which there has been a lot of interest in finding a way to solve the problem of the distribution of medical care more equitably both for the patient and for the doctor. The White Cross Plan, sponsored as an experiment along these lines, aroused a great deal of comment, and subsequently the Massachusetts Medical Society launched the Blue Shield Plan. It is to be hoped that the latter, which admittedly gives only partial coverage at present, will continue to evolve until far more adequate service is provided.

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1. *A National Health Service* A statement by the Ministry of Health and the Department of Health for Scotland. 85 pp New York: The Macmillan Company, 1944
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Meningitis, meningococcal, was reported from: Abington. 1; Braintree. 2; Boston. 8; Chelsea. 1; Fall River. 1; Fitchburg. 1; Hardwick. 1; Kingston. 1; Leominster. 1; Malden. 1; Middleboro. 2; Palmer. 1; Westfield. 1; total. 22.

Meningitis, Pfeiffer-bacillus, was reported from Lee. 1; Westfield. 1; Salem. 1; total. 3.

Meningitis, pneumococcal, was reported from: Cambridge. 1; total. 1.

Meningitis, other forms, was reported from: Boston. 3; total. 5.

Salmonella infections were reported from: Attleboro. 1; Boston. 1; Cambridge. 1; Everett. 1; Lynn. 1; Melrose. 1; Newburyport. 1; Pittsfield. 1; Walpole. 1; Waltham. 1; Watertown. 1; Wellesley. 1; West Stockbridge. 1; Worcester. 1; total. 15.

Septic sore throat was reported from: Amesbury. 1; Arlington. 1; Boston. 4; Cambridge. 1; Fall River. 1; total. 8.

Tetanus was reported from: Boston. 1; Medway. 1; Pittsfield. 1; Wareham. 1; total. 4.

Trachoma was reported from: Arlington. 1; total. 1.

Trichinosis was reported from: Andover. 1; Boston. 2; Brookline. 1; Falmouth. 1; Melrose. 1; total. 6.

Typhoid fever was reported from: Tewksbury. 1; total. 1.

Typhus fever was reported from: Camp Myles Standish. 1; total. 1.

Undulant fever was reported from: Boston. 2; total. 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	December 1	Albert H. Brewster
Salem	December 4	Paul W. Hugenberger
Haverhill	December 15*	William T. Green
Brockton	December 14	George W. Van Gorder
Worcester	December 15	John W. O'Meara
Pittsfield	December 18	Frank A. Slowick
Fall River	December 18*	Eugene A. McCarthy
Hyannis	December 19*	Paul L. Norton
Springfield	December 20	Garry deN. Hough, Jr.

*Day changed.

MISCELLANY

ATYPICAL PNEUMONIA SIMULATING PULMONARY TUBERCULOSIS

A new disease of the respiratory tract has captured a place on the medical scene during the past decade. Primary atypical pneumonia — to give it the name that seems most commonly used — has probably existed for years masquerading as atypical influenza or gripe. With the increasing use of x-ray films in diagnosis the prevalence of the disease has begun to emerge, and its importance to be recognized. The danger would now appear to be that it is as yet incompletely differentiated from pulmonary tuberculosis and that, unless progress film studies are carried out, some cases of tuberculosis will be treated for pneumonia and some cases of pneumonia given tuberculosis therapy. The following is an abstract of a paper (Yoskalka, J. S. A typical pneumonia simulating pulmonary tuberculosis. *Am. Rev. Tuberc.* 49:408-413, 1944) that considers this problem.

For many years it has been the teaching of the medical profession to regard a patient subacutely ill with infiltrations of the upper lung fields in x-ray films as probably tuberculous unless proved otherwise. Recently it has become apparent that atypical pneumonia can produce lesions that at times are indistinguishable from pulmonary tuberculosis. This has been reported on several occasions. With the apparent increase in the incidence of atypical pneumonia, especially since the profession is becoming more conscious of it, it is evident that criteria for a differential diagnosis of these two conditions should be formulated.

Clinical Observations

The symptoms and clinical signs of atypical pneumonia have been adequately described in the current literature. The usual gradual onset of the disease, associated with malaise, generalized aches and pains, dry, nonproductive cough and fever may be simulated by any case of acute pneumonic tuberculosis. A differential diagnosis cannot be made solely on the basis of the history and physical examination. Where serial roentgenograms are not feasible, the persistence of cough and expectoration, together with the finding of rales for a period greater than twenty-one days from the onset of the disease, should lead one to suspect tuberculosis, even though the patient appears to be much improved.

Röntgenologic Aspects

In our 7 cases of upper-lobe atypical pneumonia two types of shadows were found on the films. The most frequent was an increase in the bronchial markings manifested by linear streaking densities with superimposed mottled shadows. This was most marked at the hilum and, with an extension of the disease, spread toward the periphery of the lung fields. The other type of finding was an area of increased tissue density in the parenchyma of the lung relatively uniform throughout and resembling the shadow seen in early pleural effusion. X-ray evidence of atelectasis was found in our cases only when the entire right upper lobe was involved. Complete involvement of an upper lobe will usually reveal some associated evidence of atelectasis, whereas in complete consolidation of a lobe due to pneumonic tuberculosis this is usually not the case. Because there was such a wide divergence of roentgenologic findings in our cases of atypical pneumonia it was thought that we could not make a definite differential diagnosis from a single film. In serial x-ray studies it was observed that cases of atypical pneumonia could be expected to show complete clearing of the chest involvement in from four to twenty days. If the serial roentgenograms still reveal a density twenty days after the onset of the illness, pulmonary tuberculosis must be seriously considered even if other evidence favors an x-ray diagnosis of atypical pneumonia.

Case Reports

CASE 1. A white soldier was admitted to hospital with a 1-day history of generalized aches and pains, headache, malaise, fever and chilly sensations. The physical findings were normal except for a moderate injection of the pharynx; the temperature was 100°F., the pulse rate 82, and the respirations 20 per minute. The white-blood-cell count was 9200, with 72 per cent polymorphonuclears. The working diagnosis was influenza. The patient continued to run a fever reaching 103.8°F. 2 days later. Within 4 days he had developed a nonproductive cough. Physical examination at that time revealed suppressed breath sounds with an occasional fine moist rale in the right upper lobe. An x-ray film of the chest showed complete consolidation of the right upper lobe. This had almost completely cleared within a week's time, although the fever persisted somewhat longer. Recovery was uneventful and the patient was discharged to duty on the 20th hospital day.

Comment. This case illustrates the difficulty of making a definite diagnosis roentgenologically. Bacteriologic examinations were negative, and the rapid clearing of the lesion ruled out tuberculosis.

CASE 2. A white soldier was admitted to the hospital with a 2-day history similar to that above. The admission temperature was 101°F., the pulse rate 100, and the respirations 20 per minute. The white-blood-cell count was 6800 with 64 per cent polymorphonuclears. The working diagnosis was influenza. A film of the chest made 4 days following the onset of the illness showed marked increase in the hilar shadow with marked mottled densities throughout the right upper lobe. In one area there was a shadow with a central high light suggestive of cavitation. The film made 15 days following onset showed complete clearing of the parenchymal lesions.

Because of the x-ray film suggesting cavitation, sputum and gastric studies were made. All were found to be negative for tubercle bacilli. The patient made an uneventful recovery and was discharged on the 22nd hospital day.

the Children's Hospital, Boston, or the Division of Biologic Laboratories for study purposes.

The superiority of immune serum globulin for the control of measles has been well demonstrated, and the department has been looking forward to the time when this material would become available for general use. Once the proof of its usefulness had been established, the availability of immune serum globulin depended on the accumulation of sufficient reserves to take care of any possible needs of the armed forces. Such reserves are now on hand. The globulin is derived from blood donated by volunteers through the American Red Cross for the armed forces, and the Red Cross has made arrangements for the distribution of the surplus for civilian use as long as it is available (*J. A. M. A.* 125:638, 1944). Material so distributed will be processed at cost by the commercial firms now preparing albumin for the armed forces, and will be furnished without charge to the public through state health departments or related organizations, which will bear the expense of processing and distribution. In Massachusetts the globulin is available through this department, and distribution will begin on December 1. The immune serum globulin will in every respect take the place of immune globulin (placental extract), which the department has distributed for the past ten years as an agent for the control of measles. The distribution of placental extract has therefore been discontinued. Sodium citrate solution, which has been used as an anticoagulant in the administration of parental blood for the control of measles, is also being discontinued.

Immune serum globulin is used in the same fashion as placental extract and with the same indications, that is, for the modification of measles in an exposed healthy susceptible person three years of age or older and for the prevention of measles in exposed infants under three years of age, debilitated or chronically or acutely ill older patients or groups of susceptibles in whom a measles epidemic must be avoided.

The attention of physicians is called to the fact that the globulin is most effective when given to a freshly exposed person during the first six days after the date of exposure, although some effect may be at times obtained if it is given as late as the tenth day. The globulin does not permanently immunize a child to measles: although complete immediate protection is usually obtained to exposure, the child again becomes susceptible in three or four weeks. If, on the other hand, modified or unmodified measles occurs, permanent immunity is usually conferred by the attack. Detailed directions for use of the immune serum globulin are included in each package.

The globulin will be distributed through the usual channels — to local boards of health having approved biologic depots or directly to physicians, hospitals or other institutions unable to obtain their

needs through their local boards of health. Physicians and others obtaining supplies of this material are urgently requested to keep their orders within their probable needs for a period of two or three weeks. Since the Department has to purchase globulin, the supply is limited, and it is hoped that the available supply be distributed as equitably as possible.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1944

DISEASES	RÉSUMÉ		
	OCTOBER 1944	OCTOBER 1943	SEVEN YEAR MEDIAN
Anterior poliomyelitis	99	54	19
Chancroid	1	*	*
Chicken pox	370	485	380
Diphtheria	19	17	18
Dog bite	842	703	812
Dysentery, bacillary	32	24	24
German measles	36	82	35
Gonorrhea	438	435	416
Granuloma inguinale	0	*	*
Lymphogranuloma venereum	1	*	*
Malaria	36	16	0
Measles	276	401	373
Meningitis, meningococcal	22	40	6
Meningitis, Pfeiffer-bacillus	5	8	1
Meningitis, pneumococcal	1	4	†
Meningitis, staphylococcal	0	0	†
Meningitis, streptococcal	0	0	†
Meningitis, other forms	3	0	†
Meningitis, undetermined	0	13	†
Mumps	350	158	199
Pneumonia, lobar	159	161	219
Salmonella infections	15	14	4
Scarlet fever	459	622	572
Syphilis	408	380	424
Tuberculosis, pulmonary	249	225	256
Tuberculosis, other forms	17	12	29
Typhoid fever	1	4	6
Undulant fever	2	6	5
Whooping cough	287	321	420

*Made reportable in December, 1943.

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941

COMMENT

No unusual trends are indicated by the figures for October. The usual seasonal increase of several of the diseases has not as yet become marked enough to indicate which are likely to be high during the coming year. Measles and scarlet fever are unusually low because of the downward swing after two years of high prevalence.

Poliomyelitis during October, although still much above the seven-year median, showed a marked decrease from the August and September prevalence. The usual seasonal drop to a very low level may be expected in succeeding months.

Meningococcus meningitis continues to run well below last year's level, although still above the seven-year median. The same is true, to a lesser degree, of scarlet fever.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Amherst, 1; Arlington, 2; Barre, 2; Beverly, 1; Boston, 16; Boylston, 1; Brockton, 2; Brookline, 1; Cambridge, 1; Chelsea, 1; Chicopee, 6; Dedham, 1; Everett, 1; Fitchburg, 1; Framingham, 2; Greenfield, 1; Hancock, 1; Hanover, 1; Haverhill, 1; Hingham, 2; Lee, 1; Ludlow, 2; Lynn, 1; Medford, 1; Natick, 2; Newburyport, 1; Newton, 6; Orange, 1; Pepperell, 1; Pittsfield, 15; Reading, 3; Revere, 2; Somerville, 1; Springfield, 1; Stockbridge, 1; Swampscott, 1; Waltham, 1; Watertown, 2; Webster, 1; Weymouth, 2; West Brookfield, 1; West Stockbridge, 1; Worcester, 6; total, 99.

Diphtheria was reported from: Boston, 3; Cambridge, 2; Everett, 1; Lowell, 5; Somerville, 7; Worcester, 1; total, 19.

Dysentery, bacillary, was reported from: Billerica, 1; Boston, 4; Fall River, 6; Lexington, 8; Lowell, 1; Malden, 5; Medford, 2; Peabody, 1; Plainville, 2; Somerville, 1; Stoneham, 1; total, 32.

Encephalitis, infectious, was reported from: Springfield, 1; total, 1.

Malaria was reported from: Boston, 1; Cambridge, 2; Camp Edwards, 4; Chelsea, 2; Chicopee, 1; Cushing General Hospital, 20; Lowell, 1; Peabody, 1; Revere, 1; Somerville, 1; Waltham, 2; total, 36.

depressing metabolism and allaying fear. Unfortunately, in doses large enough to produce amnesia it frequently causes respiratory depression. By the addition of scopolamine in doses as low as 1/200 gr.) the patient can frequently be rendered amnesic for the period immediately before the trip to the operating room and for his stay there. Scopolamine has the effect of producing a "don't care" state of mind even though the patient may be quite alert. Furthermore, scopolamine is as effective as, if not superior to, atropine in inhibiting secretions from the mucous membranes. Since this drug does not cause respiratory depression in therapeutic doses, it is an excellent adjuvant to morphine for preoperative medication. The addition of small doses of a barbituric acid derivative (2 gr. of Sodium Luminal in the case mentioned) frequently helps to render the patient unconscious during the operative procedure.

In the editorial it is stated that fifteen minutes after the administration of the anesthetic agent, the anesthetist was busy giving artificial respiration and the nurse was giving coramine subcutaneously. It is hard to understand how this respiratory difficulty could have been due to the preoperative sedation with the patient breathing twelve to fifteen times a minute after what was probably a brief operative procedure. It would also seem that a drug depression serious enough to require artificial respiration would have been noted before the anesthetic was given.

From the small amount of information given in the article it seems a much likelier conclusion that the spinal anesthetic agent had progressed far enough cephalad to paralyze some or all of the intercostal muscles or even the diaphragm, and by the time the operation was completed, this paralysis had worn off sufficiently to permit spontaneous respiration. If this conclusion is correct, the administration of the coramine was superfluous, since the only effective treatment for this condition is artificial respiration after the establishment of an adequate airway.

The proportions of the various drugs used for preoperative sedation have been arrived at after very careful pharmacologic and clinical research. It is quite obvious that the ideal dose cannot always be selected and that there will always be some patients in whom the effect produced by the preoperative sedation will be too profound, as well as some for whom the ordered dose will be insufficient. Fortunately, in the hands of experienced anesthesiologists who are able to recognize quickly the signs of undersedation and oversedation, as well as the effects of spinal anesthetics that have gone too high, the ill effects of these inadvertent administrations can be taken care of without danger to the patient or impairment of the surgeon's work.

It is to be hoped that the opinion expressed by the author of the editorial in question does not represent the consensus of a large group of surgeons. I am sure that such an attitude can but tend to reflect discredit on an important medical specialty, and indirectly be disadvantageous to patients undergoing surgical procedures.

URBAN H. EVERSOLE, M.D., *Director*
Department of Anesthesia

Lahey Clinic
Boston

To the Editor: It is the opinion of the undersigned that several of the statements and implications made in the editorial entitled "Polypharmacy and Anesthesia" appearing in the August 3 issue of the *Journal* are misleading.

The writer of that editorial "wonders how the anesthetist knows that 1/200 gr. of scopolamine is going to contribute to the success of the anesthesia." He further states that the anesthetist should "limit himself to a moderate dose of a sedative, together with a suitable dose of atropine or some substance having the pharmacologic effect of atropine."

A little reading in preparation for the editorial would have disclosed that scopolamine is a valuable sedative and that it effectively counteracts the respiratory depressant action of morphine if given in proper dosage. A short perusal of a text on pharmacology would have revealed that scopolamine in fact does have many of the valuable pharmacologic effects of atropine.

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The editorial recommends that the surgeon, in order to protect his patient, consult with the anesthesiologist in detail concerning each step of medication given before, during and after operation. It is certainly to be hoped that the surgeon will consult with the anesthesiologist in detail about each patient about to undergo anesthesia and surgery. For the better and fuller protection of the patient, I suggest that the surgeon choose a thoroughly qualified anesthetist and depend on the anesthesiologist's more thorough knowledge of sedatives to safeguard the patient against accidents. There is no clinician more familiar with the pharmacologic action of narcotics and hypnotics than the anesthesiologist.

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Nevertheless, it should still be pointed out that there is a large body of medical opinion, found perhaps more among surgeons than among anesthetists, that simplification of premedication is a goal to be sought in future advances in anesthesia. Although the excellent human experimental work of Waters and his associates referred to in the letter from the group of Boston anesthetists has indicated that combinations of morphine and scopolamine and of Pentobarbital Sodium and scopolamine are useful and, in moderate doses, safe, there are no similar studies in which the triple combination of morphine, scopolamine and a barbiturate has been given. In fact, as indicated by Dr. Saklad's letter, some anesthetists do not approve a combination of a long-acting barbiturate and morphine in premedication.

The discussion evoked by the editorial can do nothing but good. If it can be followed up by additional experimental work and by careful observation and analysis of large numbers of cases, it may be possible to work out a universally acceptable simple form of premedication for the less intricate operative procedures in healthy patients. — Ep.

BOOK REVIEWS

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Summary

Atypical pneumonia may simulate pulmonary tuberculosis both clinically and roentgenographically, and the reverse is equally true.

Approximately 7 to 10 per cent of atypical pneumonias have upper-lobe involvement, which is the usual site for pulmonary tuberculosis.

Serial roentgenograms showing apical lesions failing to clear in twenty days following the onset of the disease should raise the suspicion of pulmonary tuberculosis.

Sputum studies for tubercle bacilli are indicated in all doubtful cases.

If lesions persist for twenty days from the onset of the illness, and routine sputum studies are negative, further studies should be done, that is, sputum and gastric concentrates and guinea-pig inoculation.

Because of the apparent increase in the incidence of atypical pneumonia, the need for an early differential diagnosis is imperative. — Reprinted from *Tuberculosis Abstracts* (November, 1944).

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"POLYPHARMACY AND ANESTHESIA"

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To answer these queries in order: The anesthesiologist knows from his clinical experience and from his knowledge of pharmacology that 1/200 gr. of scopolamine will probably contribute to the success of spinal anesthesia. One quarter or one third of a grain of morphine would not achieve approximately the same effect, because the pharmacologic effects of morphine differ fundamentally from those of scopolamine. It could be said that the Sodium Luminal (phenobarbital) is not absolutely necessary, but it contributes to the comfort and safety of the patient.

The combination and dosage of the three drugs mentioned, far from being "a practically fatal combination of sedatives," is commonly prescribed by anesthesiologists and is well within the limits of safety. Each is employed for a definite purpose. The barbiturate, in addition to its soporific effect, protects against possible toxic reaction to the local anesthetic drugs. Goodman and Gilman¹ state: "Soporific doses of the

barbiturates are only slightly depressant to the respiration; [while] morphine is a primary and continuous depressant of respiration by virtue of a direct action on the respiratory center. The effect is discernible with small doses insufficient to produce sleep or disturb consciousness. The action is a highly selective one, and the depression is directly proportional to the dose."

Sedation produced by the combination of the two drugs in moderate dosage results in less respiratory depression than would result from a large dose of morphine alone.

Scopolamine, although apparently considered by the writer of the editorial as a sedative, in reality belongs to the atropine group of drugs. We again quote Goodman and Gilman:² "Scopolamine, like atropine, has a potent inhibitory action on secretions, but in addition, the alkaloid is also a depressant of the central nervous system and reduces excitement. Scopolamine is often viewed as a respiratory depressant, but this action on the medullary center has been exaggerated. Indeed strong evidence from clinical experiments of Waters and his associates² indicates that the depression of breathing by morphine can be completely counteracted by doses of scopolamine, so that otherwise poisonous amounts of morphine may be administered to man without lowering the normal respiratory exchange."

It appears unprofitable to discuss the opinions expressed in the latter part of the editorial. We hope that the opening paragraph better reflects the beliefs of the majority of members of the medical profession: "The scientific advances in anesthesia in the last decade have been truly spectacular, and largely because of them, surgeons have been able to operate successfully in many regions of the body previously inaccessible. Furthermore, the safety of other operative procedures has been increased by these new methods, provided they are expertly applied."

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The editorialist seemed most concerned about what he considered to be too much preoperative sedation administered to a certain patient. One-sixth grain of morphine, 1/200 gr. of scopolamine and 2 gr. of Sodium Luminal could not be considered heavy medication for a healthy, seventeen-year-old male patient. It seems that the scopolamine was the drug considered to be the offender.

Since the editorial betrayed little appreciation of the purpose of preoperative medication and the action of the respective drugs used, a few words on the subject appear appropriate. The ideal premedication should allay the patient's fears of the operating room and produce a state of relative amnesia for the period. Furthermore, if an inhalation anesthetic is to be used (and this sometimes has to be resorted to even when not planned), the preoperative medication should lower the metabolic rate in order to facilitate induction and lessen the amount of anesthetic agent required to obtain the desired level of anesthesia. The preoperative medication should do all of this without sufficiently depressing respiration as to slow the absorption of the anesthetic agent and of oxygen or to predispose to postoperative pulmonary complications because of this depressed respiration and obtunded cough reflex. Morphine is an excellent drug

depressing metabolism and allaying fear. Unfortunately, in doses large enough to produce amnesia it frequently causes respiratory depression. By the addition of scopolamine doses as low as 1/200 gr.) the patient can frequently be rendered amnesic for the period immediately before the trip to the operating room and for his stay there. Scopolamine the effect of producing a "don't care" state of mind even though the patient may be quite alert. Furthermore, scopolamine is as effective as, if not superior to, atropine in inhibiting secretions from the mucous membranes. Since this drug does not cause respiratory depression in therapeutic doses, it is an excellent adjuvant to morphine for pre-anesthetic medication. The addition of small doses of a barbituric acid derivative (2 gr. of Sodium Luminal in the case mentioned) frequently helps to render the patient unconscious during the operative procedure.

In the editorial it is stated that fifteen minutes after the administration of the anesthetic agent, the anesthetist was giving artificial respiration and the nurse was giving amine subcutaneously. It is hard to understand how this respiratory difficulty could have been due to the preoperative atropine with the patient breathing twelve to fifteen times a minute after what was probably a brief operative procedure. It would also seem that a drug depression serious enough to require artificial respiration would have been noted before the anesthetic was given.

From the small amount of information given in the article seems a much likelier conclusion that the spinal anesthetic agent had progressed far enough cephalad to paralyze some of all of the intercostal muscles or even the diaphragm, and at the time the operation was completed, this paralysis had worn off sufficiently to permit spontaneous respiration. If this conclusion is correct, the administration of the coramine is superfluous, since the only effective treatment for this condition is artificial respiration after the establishment of an adequate airway.

The proportions of the various drugs used for preoperative anesthesia have been arrived at after very careful pharmacologic and clinical research. It is quite obvious that the ideal dose is not always to be selected and that there will always be some patients in whom the effect produced by the preoperative atropine will be too profound, as well as some for whom the desired dose will be insufficient. Fortunately, in the hands of experienced anesthesiologists who are able to recognize quickly the signs of underdosage and overdosage, as well as the effects of spinal anesthetics that have gone too high, the ill effects of these inadvertent administrations can be taken care of without danger to the patient or impairment of the surgeon's work.

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BOOK REVIEWS

The Permeability of Natural Membranes. By Hugh Davson, D.Sc., and James F. Danielli, D.Sc., A.I.C. With a foreword by E. Newton Harvey, Ph.D. 8°, cloth. 361 pp., with 73 illustrations and 72 tables. New York: The Macmillan Company, 1945. \$4.75.

The great usefulness of this book will be obvious to all students of biology. The authors present a general survey of the field of permeability, including materials essential for students of medicine, physiology, biochemistry, zoology and botany. It is made clear that permeability studies have passed beyond the preliminary exploratory stage, having

reached the stage at which quantitative analysis is of dominant importance. In the foreword, Professor E. Newton Harvey, of Princeton University, writes in part: "Just as chemistry could not have developed without test tubes to hold reacting substances, so organism could not have evolved without relatively impermeable membranes to surround the cell constituents. This barrier between the inside and the outside, the inner and external world of each living unit, has been and always must be considered one of the fundamental structures of a cell." Each of the twenty-one chapters is followed by a series of references, and an excellent index is provided. The last chapter deals with the theories of cell permeability.

Traumatic Injuries of Facial Bones: An atlas of treatment. By John B. Erich, D.D.S., M.D., and Louie T. Austin, D.D.S. In collaboration with the Bureau of Medicine and Surgery, United States Navy. 12°, cloth, 600 pp., with 333 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. \$6.00.

In this book the authors attempt to present a manual for the treatment of injuries of the facial bones. General considerations are covered in eleven printed pages. As the subtitle suggests, the book is a pictorial of treatment. The illustrations are well done, and should appear clear to the student, but many seem exaggerated in showing the nature of the wounds.

The methods of immobilizing the facial bones are described in great detail, and the authors explain many elaborate and complicated appliances for use in cases in which it seems likely that simple procedures of proved value would accomplish the same results. The book, however, is a valuable contribution to the literature on injuries of the face.

Clinical Tropical Medicine. Edited by Z. Taylor Bercovitz, M.D., Ph.D. With a foreword by Wilbur A. Sawyer, M.D. 4°, cloth, 957 pp., with 121 illustrations. New York: Paul B. Hoeber, Incorporated, 1944. \$14.00.

This book contains chapters by twenty-seven authors who are well known for their work in the field of tropical medicine. The editor of the volume, Dr. Bercovitz, has also contributed chapters on many of the important tropical diseases, including amebic dysentery, malaria and certain of the helminthic diseases.

Dr. Charles F. Craig has written the chapters on spirochetes and spirilla, except pinta and yaws, which have been covered by Dr. Howard Fox. Dr. Henry Pinkerton has dealt with the diseases caused by rickettsias; Dr. Edward B. Vedder, with the nutritional diseases; and Dr. Morris Moore, with the diseases caused by yeasts and fungi. The other authors have contributed importantly but less extensively to the volume. Most of the numerous illustrations are excellent.

The book is valuable because of the authoritative contributions that it contains, but its highest levels of quality are not uniformly sustained. Here and there can be found statements that are ambiguous, misleading or incorrect. For example, under amebiasis, it is said that food and water should be boiled "for at least thirty minutes" to destroy cysts, whereas, since amebic cysts in water cannot survive a temperature of 50°C. for more than a few minutes, prolonged boiling is needless. In the chapter on malaria, a serious error occurs: it is stated there that the sporozoites "enter the blood stream and attach themselves to the red blood corpuscles." Although it is not known what happens to the sporozoite after it passes from the mosquito into the human body, it is quite possible that the parasite undergoes important changes during the interval of several days that elapse before it makes its appearance in the red cell. Finally, in the chapter on beriberi, a distinction is drawn between beriberi and "the peripheral neuritis caused by alcohol." There is no convincing evidence that peripheral neuritis in man has ever been caused by alcohol per se, most physicians now believing that it results from a dietary deficiency that is secondary to the alcoholism.

Even though the book contains passages that are open to serious criticism, it contains much that is excellent.

NOTICES

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a. m.

MEDICAL CONFERENCE PROGRAM

Friday, December 1 — Surgical Aspects of Intestinal Infections. Dr. Jost J. Michelsen.

Wednesday, December 6 — Practical Aspects of Shock Therapy. Dr. Arthur Berk.

Friday, December 8 — Alloxan Diabetes: Clinical and pathologic findings. Dr. C. Cabell Bailey and Orville Bailey.

Wednesday, December 13 — Some Effects of Injected chrome C in Animals and Man. Dr. Samuel Prosser.

Friday, December 15 — The Cushing Syndrome. Dr. Kenneth W. Thompson.

On Monday mornings clinics will be given by Dr. Prosser. On Tuesday and Thursday mornings Dr. Thannhauser will give medical clinics on hospital cases. The medical profession is cordially invited to attend.

MASSACHUSETTS PSYCHIATRIC SOCIETY

On Tuesday, December 5, the Massachusetts Psychiatric Society will tender a dinner to Brigadier J. R. Reese, F.R.C.P., consulting psychiatrist to the British Army medical director of the Tavistock Clinic, London. It served at 6:30 p. m. at the Kenmore Hotel, Boston. Brigadier Reese will speak on the subject, "The Shaping of Psychiatry by War," and his lecture will be of importance not only to psychiatrists and physicians but to everyone interested in the present trends in psychiatry and the associated particularly in relation to the war and the postwar period.

The tickets, \$2.90 each, must be purchased on or before December 2 from Dr. Earl K. Holt, Box A, Harding, Massachusetts.

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the amphitheater of the Peter Bent Brigham Hospital on Tuesday, December 12, at 8:15 p. m.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

A clinic of the New England Obstetrical and Gynecological Society will be held at the Carney Hospital on December 9 at 9:00 a. m. in the operating room on the sixth floor. Louis E. Phaneuf, Roy J. Heffernan and Maurice O. Belson will perform gynecological operations.

At 10:30 a. m. a dry clinic will be held in the auditorium.

PROGRAM

The Repair of the Lacerated Perineum. Dr. Louis E. Phaneuf.

The Role of the Transverse Cervical Cesarean in the Management of Placenta Previa. Dr. Roy J. Heffernan.

The Management of the Third Stage of Labor. Maurice O. Belson.

Sternal Transfusions in Obstetrics and Gynecology. Meyer D. Schnall.

AMERICAN PUBLIC HEALTH ASSOCIATION

The third wartime conference and seventy-fourth annual meeting of the American Public Health Association will be held in Chicago during the week of September 17, 1945, with headquarters in the Hotel Stevens.

The Chicago program will cover subjects of interest to health officers, public-health nurses, laboratory workers, nutritionists, vital statisticians, engineers, child-health specialists, maternal-health specialists, health educators, public-health dentists, epidemiologists, industrial hygienists and others working in the broad field of health protection and promotion.

(Notices continued on page xv)

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THE STUDY OF THE PATIENT FROM A PSYCHOSOMATIC STANDPOINT*

KENNETH J. TILLOTSON, M.D.†

BELMONT, MASSACHUSETTS

AMONG the most recent advances in medicine resulting directly from the present war are the employment of the sulfonamides and penicillin to combat infection and that of blood plasma to combat shock. Both depend on their prompt use after injury, and delay may result in loss of the therapeutic opportunity. A third and comparable medical contribution may be added — the early recognition of psychoneurotic or emotional symptoms and their prompt treatment and management. Failure to recognize the nature of these emotional manifestations may mean delay in promptly and effectively treating the patient. Psychoneurotic disorders manifest themselves in the following manner: pain, headaches, nervousness, indigestion, dizziness, weakness, backaches and a host of other somatic complaints. These physical signs of emotional maladjustment are termed "psychosomatic symptoms." First aid in the form of prompt psychiatric treatment has already become as valuable to the armed forces and to the people of civilian areas under bombardment as have the quick recognition of a physical injury and the knowledge of how and where to apply a tourniquet to control bleeding.

There is a close parallel between first aid for physical casualties and that for so-called "mental casualties," also known as emotional maladjustments or nervous conditions, or, perhaps more correctly, psychoneuroses or psychosomatic reactions. The immediate treatment of these complaints — often severe or hysterical in character, and at times even constituting excited or psychotic reactions — forms a valuable therapeutic contribution, since a large percentage of patients with these previously disabling disorders are now completely cured, and considerable numbers of men in the armed forces are even returned promptly to active combat duties.

This method of treatment is called "narcosynthesis," and consists of administering Pentothal Sodium intravenously until a certain stage of narcosis is reached. When in this state, the patient re-experiences the intense emotions that were originally associated with the traumatic battle experiences

and that have been perpetuated in various stages of repression up to the moment of treatment. He actually synthesizes the emotions and memories connected with the experience. Under the influence of the drug the physician uses psychotherapy to free the patient of the intense repressed emotions that cause the neurotic symptoms, and the latter emerges from the narcosis with relief from his abnormal reactions and with new emotional drives, and returns in a state of renewed strength to a world of reality, both past and present. In certain cases in which the narcosynthesis does not produce the desired result, electric shocks may be given. Both the foregoing procedures depend on marked physiologic changes produced either chemically or electrically, as well as psychotherapy, to reverse the psychologic state of the patient. These newer methods and procedures have already altered the nature of present-day psychiatric practice, and it is probable that further and equally revolutionary changes will follow with the increasing demand for psychiatric treatment resulting directly or indirectly from the present war.

Prior to World War I, neuropsychiatric disorders were treated most unsatisfactorily and by a comparatively small group of psychiatrists and neurologists, most of whom were attached to mental hospitals. Such complaints and symptoms could not be dealt with in the forthright manner in which most medical symptoms were approached, for popular sentiment — including the attitude of the medical profession — toward nervous and mental diseases was extremely unscientific and at best depicted little understanding. In World War I, however, under the spur of necessity, there was revealed not only the frequency with which neuropsychiatric complaints occur but the high percentage of psychoses and psychoneuroses existing in the civilian population. Attention was also drawn to the psychosomatic elements that affect a large number of persons who, to be sure, are suffering from medical or surgical conditions, but whose treatment and management are severely complicated by emotional or psychoneurotic factors. There was thus introduced an entirely new field of thought, and in this

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

†Instructor in psychiatry, Harvard Medical School; psychiatrist-in-charge, McLean Hospital.

way there began the development of present-day psychosomatic studies that are applicable not only to neuropsychiatric patients but to all patients.

Twenty years ago, when many of those now in practice were medical students, psychiatry and the study of nervous disorders presented problems that seemed not only mysterious but infinitely complex. From the available literature and from the meager instruction current in medical schools at that time, it was difficult to obtain a concise and unbiased presentation of the mechanisms that underlie abnormal behavior and emotional disorders.

The professional vernacular presumed an acquaintance with much, although it was not a part of ordinary experience, and in lieu of actual experience with neuropsychiatric disorders as then understood, a few stereotyped descriptions of the vintage of Janet, Charcot, Babinski and Kraepelin served to give an understanding of neurologic and psychiatric disorders, together with equally unsatisfactory descriptions of the end stages of manic-depressive psychoses and dementia praecox. The medical profession as a whole had not as yet discovered the importance of the dynamic and emotional factors in psychologic medicine, nor did it realize that the psychologic components — namely, the emotional factors and neuropsychiatric disorders as such — were frequently not considered or missed in diagnosis. This state of things resulted in much unnecessary chronic illness, to say nothing of an immense amount of needless surgery.

The psychogenic hypothesis was first outlined by Brodie as long ago as 1837. It stressed the importance of the unconscious to the development of personality and to subsequent emotional experience — a subject that was later presented and elaborated by Freud, Jung and others. Generally speaking, twenty years ago little was known about psychodynamics, psychopathology and psychobiology; all of which means that nothing was known, practically speaking, of the tremendous field of the unconscious and its relation to the causes of psychoneuroses, the importance of psychosomatic relations and the early emotional manifestations and symptoms of all disease or illness.

In World War I, psychiatry began to be recognized as having an important contribution to make. For the first time it was given, although reluctantly, a place of slight responsibility along with the other medical specialties. With the development of post-war psychiatric problems in returning veterans, neuropsychiatric disorders began to be placed on a responsible medical footing. It remained for a better understanding of psychosomatic medicine and its integration with the daily practice of general hospital medicine to demonstrate its value. From the application of physiologic principles, together with a psychologic understanding of the patient, successful treatment of psychoneurotic disorders became an accomplished fact, and the field of neuro-

psychiatry could be said to stand on a firm scientific basis and from a clinical standpoint to compare favorably with other specialties.

How does this relate to the problems of mental health in the present armed forces and the mental health of the civilian population under the stress of the present war? It is frequently asked what the psychologic effects of war are on civilians and military personnel, whether the war has developed any new types of nervous and mental disorders, and whether present-day neuropsychiatrists and the medical profession in this country are adequately equipped to handle such conditions. The final answer rests on the ability of the medical profession to practice psychosomatic medicine and to face intelligently the ever-increasing emotional factors and their influence on personality as well as on the patient's physiologic state.

The psychologic effect of war on civilians and soldiers and sailors may be disastrous in that predisposed tendencies may become activated and emotional symptoms, a neurosis, a psychoneurosis or even an actual psychosis may develop. That these disorders are no different from the prevailing disorders of the last war, psychiatrists seem to agree. The so-called "shell shock" of World War I might be anything from a neurosis to a psychosis of the most profound character. The exhaustion or fatigue syndromes of the present war and the psychosomatic complaints are again a mere repetition of psychoneurotic complaints, varying in manifestation, intensity and duration and also in response to treatment, depending largely on the constitutional factors in the given patient. That there are not enough psychiatrists at the present time to deal with the vast number of neuropsychiatric casualties in the armed forces is evidenced from all quarters. For instance, some time ago a bulletin from the War Department stated that any medical officer might be called on to treat neuropsychiatric casualties because of the shortage of psychiatrists. The burden of treating these casualties will fall on medical officers without specialized training. This fact may be more vividly portrayed by the following figures. An average of 8 to 20 per cent of the men examined for military service are rejected for psychiatric reasons, and 40 per cent of the discharges from the armed forces are made for psychiatric reasons. In contrast, about 2 per cent of the members of the medical profession are neuropsychiatrists. In addition, one third of the neuropsychiatrists in this country are now in the armed forces. The social implication of these figures is enormous, but their importance to the medical profession and to the general practitioner is even greater and more challenging. Every physician is aware of the fact that even in peacetime 40 to 60 per cent of the patients seeking medical help present essentially emotional problems or frank psychiatric disorders. A major result of the war experience is the compelling necessity to focus at-

attention on a large section of the population who need medical care and who previously may not have recognized this need. No doubt there will also be a considerable increase in the number of patients with disabling functional illnesses seeking help from every specialty of the medical profession.

The most frequent diagnosis of these disabilities by far is that of psychoneurosis — a term that connotes a great number of clinical entities. Unfortunately, ordinary neuropsychiatric disorders have been thought to occur only in those with personality defects or, generally speaking, in weaklings. This is not true. A fair proportion of neuropsychiatric patients give no history of previous difficulties. Under the extremes of fatigue and the stress of modern combat, the most stable person may reach his breaking point. Thus the presence of neuropsychiatric disorders in combat must be looked for in the normal persons as well as those predisposed to such abnormal states.

In soldiers, the factors that precipitate emotional disorders with resulting psychosomatic symptoms include separation from home, regimentation, lack of freedom, lack of privacy, lack of feminine companionship, a feeling of not being appreciated and a lack of confidence in leaders. In combat, there are extreme fatigue, danger and long exposure to death, malnutrition, exposure to heat and cold, disease, isolation, confusion, hunger and the fear of being a coward or of losing one's self-control, as well as the realization of the responsibility for the lives of others, insufficient understanding of war or lack of the conviction to fight.

A distinction may well be made between the treatment and the management of psychoneuroses. Treatment depends on the type of disorder and its duration, the ability of the physician and the degree of rapport that is developed between him and the patient. Obviously a great many patients are treated without being cured. Probably few psychoneurotic subjects are treated by competent physicians without being relieved. The result obviously depends not only on the method of treatment and the ability of the therapist, but on the type of patient and the nature of the psychoneurosis.

If the study of psychosomatic factors and the approach to the patient are correct, the only rational method of treatment consists in the revealing to him of the unconscious mental processes that are responsible for the symptoms or illness as a whole, by bringing into consciousness the repressed impulses that find vicarious satisfaction in symptoms. The patient must be given an insight into why he has symptoms and how they are produced and what they mean at the psychologic or psychobiologic level, and must be shown that nervousness and emotional tension result from conflicts and frustrations. In some cases this is relatively easy. In many others, however, it is extremely difficult, because

therein lies the crux of the problem. Many psychoneurotic patients are highly intelligent and see the surface problem together with its ramifications and implications, yet are utterly at a loss to resolve it.

A psychoneurosis is not a matter of logic, and no amount of intellectualization will cure a state that is emotionally so deeply conditioned. Adjustment is not always or even generally possible, not alone because many of the inner emotionally toned conflicts are difficult to discover and resolve, but because most of the social and environmental factors are beyond the control of the therapist and many beyond the ability of the patient to mold to his own needs. If, however, the basic personality patterns cannot be changed, the patient may get relief through appreciation and understanding of the true nature of the illness.

Take, for example, a patient recently under treatment who had a typical neurasthenic type of psychoneurosis. A physician told her that the weakness and low blood pressure were indicative of a pituitary syndrome. He gave her many hormones and endocrine substances and had her remain in bed for months, but finally accomplished a fairly satisfactory shock treatment by telling her one day, "Of course you might as well know you have a serious pituitary disorder, Simmonds's disease, and you will gradually become a completely bedridden invalid." She was naturally quite overwhelmed and finally asked for a consultation. She was sent to a Boston hospital where an internist decided that she did not have the serious pituitary disorder, and ordered her out of bed. He informed her, however, that she did have a nervous disorder and referred her to a psychiatrist. Soon afterward she consulted me. Her co-operation in a reasonably active program, even including housework, which she had been told she would never be able to do, was excellent. More obvious conflicts, such as an incompatible sex relation with her husband occasioned by fear of pregnancy due to a severe and near fatal post-partum hemorrhage following her last childbirth, along with many other emotional problems, have been worked out. The development of a proper and hygienic routine of life and reassurance and definite proof that she can live an active, useful life constitute an improved state, and furnish a good example of the management of a psychoneurotic patient of the neurasthenic type.

Many acute tension and anxiety states must be dealt with on a symptomatic basis while the deeper and more fundamental psychologic factors are being explored. This necessitates management. If employment is cut off, a program of occupational therapy or physiotherapy and exercise must be instituted, unless a period of rest and heavy sedation is indicated. Small doses of drugs or refraining from the use of drugs is the safest policy unless a period of sedation is for some reason believed de-

sirable for the patient's immediate needs. In many cases chemotherapy enhances the value of psychotherapy.

An important point in the management of psychoneuroses is that the patient with psychogenic pain, headaches, insomnia, vomiting, tremors or feelings of tension, and combinations of these, believes that the symptoms are as real as an organic disease. Indeed, most patients insist that they would rather have pneumonia or surgical conditions requiring operation than this so-called "nervousness."

A patient with anxiety hysteria or obsessional states has a real illness, and reassurance may be of little value. He fears insanity, death, cancer, syphilis or some lingering disease. I treated periodically for several years a neurotic patient with the obsession that he had syphilis. Hinton tests and reassurance by a formidable array of outstanding medical consultants only gave him possible loopholes as he played one against the other. After a detailed medical, social and somewhat psychoanalytical approach through periods of free association, and after thorough physical examinations, it was finally discovered that at the age of twelve or fourteen the patient caught his mother in a sexual act with a man whom he later heard had syphilis. The emotional shock of the affair and his strong dislike for the man, together with the fact that his father had divorced the mother several years later because of her infidelity, made him build up a long and varied train of extremely painful conflicts. These revealed themselves in a real neurosis when he married, and his own marital situation suddenly overwhelmed him when he recalled an experience he had had in college with a prostitute while under the influence of alcohol. His long developing doubts and emotional conflicts were first manifested in anxiety; he then became fearful that he had contracted syphilis. When the steps of this development had been shown to the patient, he became much better. In fact, he made a good recovery over a period of two or three years, with several interruptions of otherwise fairly constant therapy.

To be successful, then, treatment must be directed to the individual problems of the patient and should reckon with his special personality profile. Psychotherapy actually begins the moment the patient enters the office, and both a detailed psychologic study and a careful physical examination are directed to that end. The physical examination, in particular, not only is useful for the purpose of excluding organic disease but serves as an excellent therapeutic measure in that it convinces the patient that his complaints are being seriously considered.

Nonne¹ wrote, "The war has shown that persons with a previously sound nervous system can acquire a neurasthenia complex, and hysteria is no rarity in war, even in persons hitherto quite healthy." An illustration of this fact is furnished by the ex-

perience of an officer from an American cruiser who had recently returned from the Mediterranean theater. Recounting his experiences in connection with his own neurotic disorders, he told of an experience concerned with the picking up of a transport plane in the Sicilian campaign. When the paratroopers in the plane had been commanded to jump, all had done so except an eighteen-year-old soldier. The officer leveled his revolver at the boy, who said, "Go ahead and shoot—I can't jump." When the paratrooper came aboard the cruiser, he wept hysterically, just as he had been seized with extreme terror and fright, which resulted in a complete numbness and inability to jump, when ordered to bail out, although always before in training he had experienced no trouble. The effect of this situation on the ensign was closely identified with his own anxieties and fears. The ensign wept bitterly and denounced the officer. "That yellow . . . tongue-lashed and threatened the poor kid all the way back to Africa amidst the suffering and groans of a boatload of wounded men." The ensign, who was on active duty, had consulted me believing he should resign from his naval post and return to civilian life to take up the study of medicine, since doctors were so badly needed. He thought that he could return to the front after completing his medical education and really do some good.

The outstanding cause of psychoneuroses, apart from a predisposition under actual service conditions, is undoubtedly fear of death or disablement. The symptoms exist because the patient is afraid, and they persist so long as there is any conflict between a desire for self-preservation and a sense of duty. If he is removed from duty permanently or if he refuses point-blank to face danger again, even to the extent of facing the disciplinary action or consequences that may be in store for him, he loses his symptoms, sometimes in a few hours. Other factors that have been alleged, such as guilt over killing, are infinitely rarer.

The psychosomatic study of the patient should begin with the complaint problem or the presenting symptoms. The underlying personality profile and emotional factors lead to evaluation of the part played by these emotions and anxieties in the development of the bodily symptoms. Queer behavior or conduct disturbances are not alone caused by psychologic or emotional factors. A review of recent publications in the field of psychosomatic medicine reveals that there is practically no physical disease or illness that is not caused or complicated by psychologic factors. This has been repeatedly demonstrated in such ordinary medical conditions as peptic ulcer and anorexia nervosa. The latter has been described as a psychosomatic entity, and in fact practically every medical disease is precisely that.

The psychosomatic approach must therefore take into consideration that the patient is a human

being with worries, fears, hopes and despairs, with the psychologic means of unconsciously converting these emotions into physical symptoms or of otherwise modifying the body physiology. This is most strikingly demonstrated in affective disorders, that is, in depressive states, from reactive depressions to manic states and involutional melancholia. A recent review of the results of electric-shock treatment of the foregoing disorders at the McLean Hospital not only demonstrates outstanding therapeutic results as compared to a control group treated without the aid of electric shocks, but clearly demonstrates the reversibility of the emotional or psychologic symptoms, with simultaneous dramatic changes in the body physiology.² The precise nature of these changes is not exactly understood, but the psychosomatic relations have been clearly demonstrated.

It may be of interest to note a few of the results of electric-shock treatment in a series of 70 patients with depressive states, as compared with a control group of patients suffering from the same types of depression but treated without electric shock. Eighty per cent of the treated group showed remission, as against 50 per cent of the control group. The quality and permanence of recovery in the shock group was almost twice as high as in the

other group, and the hospitalization of the former group varied from one to two months — 90 per cent less than that in the control group.

* * *

Psychiatrists have utilized the psychosomatic study of patients to a far greater extent since the use of the various shock therapies were introduced about ten years ago. The concept of the study and treatment of the personality as a whole on an individual basis has been one of the most important contributions of psychiatry to general medicine. Since physicians are now being called on to treat and manage an increasing number of psychoneuroses, as well as emotional states manifested by psychosomatic symptoms in a variety of illnesses, these psychosomatic considerations should be more widely accepted, utilized and integrated into the daily practice and experience of the general practitioner.

REFERENCES

1. Nonne. Cited by Dunbar, H. *Emotions and Bodily Changes: Survey of literature on psychosomatic interrelationships*. 595 pp. New York: Columbia University Press, 1935. P. 374.
2. Tillotson, K. J., and Sulzbach, W. Comparative study and evaluation of electro-shock therapy in depressive states. *Am. J. Psychiat.* (in press).

PILONIDAL CYST

An Analysis of 132 Consecutive Cases

LIEUTENANT COLONEL H. H. HAMILTON, M.C., A.U.S., LIEUTENANT COLONEL B. S. CUSTER, M.C., A.U.S., AND CAPTAIN A. KELLNER, M.C., A.U.S.

THIS study of the problem of pilonidal cyst is based on a review of 132 consecutive cases discharged from a station hospital from July 1, 1942, to October 1, 1943 — a fifteen-month period. At the beginning of the study, a method of preoperative classification and grading of cases was worked out. A policy was set and maintained throughout not to release a patient to duty until healing was complete. Various types of operations have been used during the study of this series of cases. Conclusions were reached after analyzing the first 66 operated cases. The preoperative classification of cases adopted was as follows:

Grade 1. On examination, the patient presents a sinus or sinuses and a palpable tumor, but there is no history of inflammation, that is, no local pain, swelling or discharge. If the case has been properly graded, the report of the pathologist indicates only fibrosis and giant-cell reaction, with minimal round-cell infiltration.

Grade 2. The patient presents a history of discharge and recurrent local tenderness and swelling, but not within the eight weeks prior to examination. Pathologically, the lesion of this grade of case shows chronic inflammation, as evidenced by a plasma-cell and lymphocytic-cell reaction.

Grade 3. The patient presents a history of recurrent discharge or previous abscess formation requiring drainage, or both. At the time of admission examination reveals local induration and tenderness. Pathologically, the lesions in these cases show acute and chronic inflammation, as evidenced by infiltration with neutrophils, lymphocytes and plasma cells.

Grade 4. At the time of examination the patient presents acute suppuration and abscess formation. Pathologically, there is gross pus and necrotic tissue.

Grade 0 (included for completeness). These cases are frequently referred for attention and are subclinical in type. Examination reveals a sacrococcygeal dimple that is completely epithelialized and contains no tumor mass at the bottom of the dimple. The tip of the coccyx invariably curves posteriorly, a point of great assistance in differential diagnosis. (In reviewing this series of 132 cases a single case of Grade 0 was noted; this was improperly classified as Grade 1 and failed to disclose any cyst on microscopic section.)

In arriving at the proper preoperative grading, white-cell and differential counts were of no benefit. Determinations of the erythrocytic sedimentation rate were also of little value. In borderline cases exhibiting no other evidence of disease within the previous three weeks, the sedimentation rate was of some value in so far as a rate above 10 mm. per hour by the Wintrobe method or above 15 mm. per hour by the Westergren technic, without any complicating disease, indicated that a careful, close study of the specimen should be made before the type of closure was decided on. Studies of frozen sections were carried out in a few cases of this type, but cutting of the cyst is difficult and the procedure is impractical. In order of importance, the results of physical examination, the history and the laboratory findings are the three items used in determining a grade.

This series was preoperatively graded as follows: Grade 1, 45 cases; Grade 2, 24 cases; Grade 3, 45 cases; Grade 4, 9 cases; ungraded, 9 cases. Four of the 9 ungraded cases did not come to operation because of separation from the service for other defects or a history of cysts that had been previously operated on, with breakdowns.

TYPE OF OPERATION

In evaluating this problem, 128 cases were considered since, as stated above, 4 of the ungraded cases did not come to surgery. The 5 remaining ungraded cases were all treated by excision and packing.

Excision and primary closure. This was done in 43 Grade 1 cases, with 1 failure (2 per cent); in 20 Grade 2 cases, with 2 failures (10 per cent); in 19 Grade 3 cases, with 10 failures (53 per cent); and in none of the Grade 4 cases. Failure is defined as any primary closure that required reopening or that on follow-up examination showed tissue breakdown or evidence of recurrence. The procedure of Ferguson and Mecray¹ (Figs. 1 and 2) was followed, with only minor modifications. With the patient in the Kraske position, and under a low-spinal or local anesthetic, the cyst and overlying skin are excised, strict attention being given to hemostasis. No preliminary injection of dye is used, and sutures of No. 50 black cotton are used on all bleeding points and to close the subcutaneous space. Three or four vertical mattress sutures of No. 30 steel-alloy wire are used

to approximate the sacrococcygeal fascia and tied over dental cotton rolls. Sutures of No. 50 cotton are used to approximate the skin. Postoperatively the patient is encouraged to lie on his back for at least an hour, and if possible, measures are

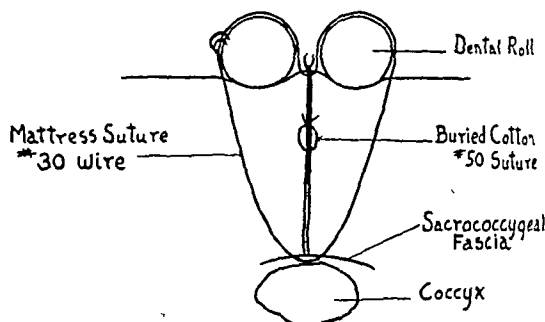


FIGURE 1. Schematic Cross Section of Modified Ferguson Operation.

taken to prevent defecation for five days to a week. The sutures are removed on the tenth postoperative day; the patient becomes ambulatory on the twelfth day and is returned to duty on the eighteenth to twenty-first day. In the 82 cases treated by primary closure, including the failures, the average time from operation to return to duty was twenty-five days.

Excision and packing. In the first 66 cases reviewed in this series 24 (37 per cent) were managed

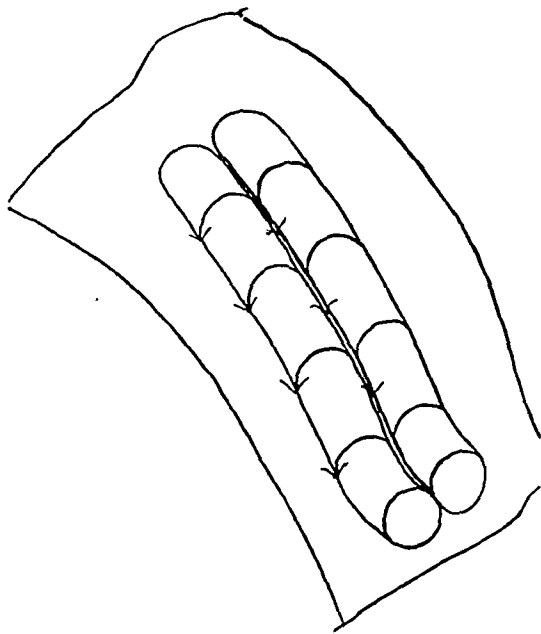


FIGURE 2. Appearance of Site at Completion of Modified Ferguson Operation.

in this manner, and the average time of hospitalization was sixty-two days. Of the remaining 62 cases, only 4 received this type of management and the average period of hospitalization was one hundred and two days. This procedure has been almost entirely supplanted by partial closure.

Partial closure. The technic used in these cases was that of MacFee² (Figs. 3, 4, 5 and 6). This type of management was used in 11 of the final group of 22 cases. Nine of these cysts were Grade 3. 1 was

and ferric chloride 1 per cent) is applied to the granulating walls with an applicator, left for two minutes and flushed out with saline solution. This is done once daily until a clean, healthy, granulating surface is presented. These patients were discharged to duty as healed on an average of twenty-seven days after operation. Small areas of recurrence are

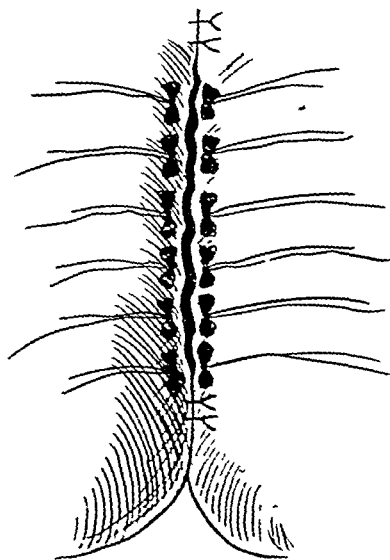
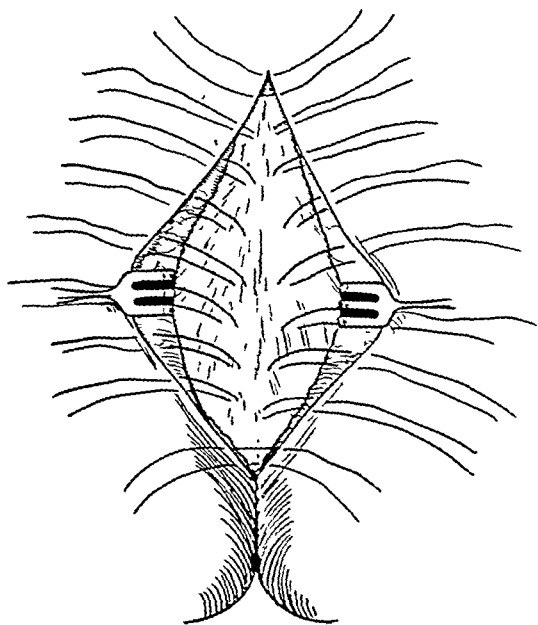


FIGURE 3. MacFee² Type of Partial Closure.

Mattress sutures of No. 20 cotton have been placed through the skin edges and fascia and are ready for tying.

Grade 4, and 1 was Grade 1, being too large for complete closure. The average time from operation to return to duty in this group was forty-five days.

Incision and drainage. This procedure was limited to 7 cases of gross suppuration and abscess formation.

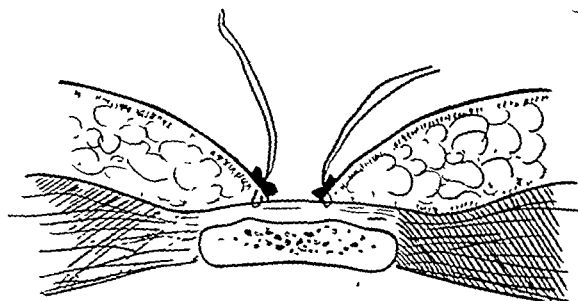
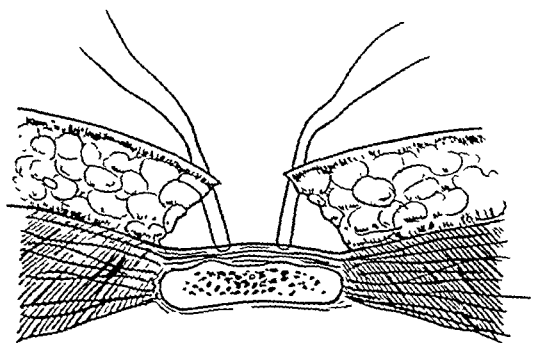


FIGURE 5. MacFee² Type of Partial Closure.

The sutures are tied over small pieces of rubber dam, bringing the skin edges to the fascia without tension. In the lower sketch, showing a cross section, note that the sutures are left long.

FIGURE 4. MacFee² Type of Partial Closure.

This represents a cross section of the partial closure.

Nearly all these lesions were quite simple in type. Incision and drainage is done at the outset, and careful use of cauterizing agents effects a cure in simple types of abscess. Care is taken to excise the fistulous tracts at the time of operation, and 3 to 5 gm. of sulfanilamide powder is inserted, followed by loose packing, which is left for a week. After this, Carnoy's solution (absolute alcohol 6 per cent, chloroform 3 per cent, glacial acetic acid 1 per cent

apt to appear in this type of case, but none has been observed in this group, some of which have been followed for more than a year.

COMMENT

Grade 1 and Grade 2 cases have been satisfactorily closed by a modified Ferguson technic. Sixty-three cases were managed in this manner with 3 known failures. After discharge to duty, all these

patients have been re-examined at monthly intervals as long as they have remained on this field, and the follow-up study has been efficient enough so that delayed failures and recurrences may be considered to be extremely rare.

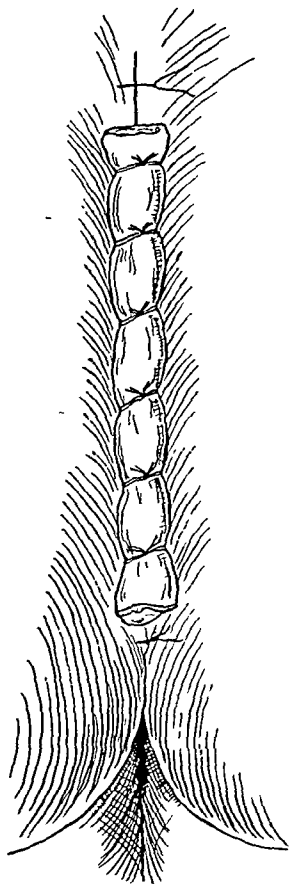


FIGURE 6. MacFee² Type of Partial Closure.

The wound is frosted with sulfanilamide powder, and the ends of the sutures are tied over a roll of iodoform gauze. This is covered with a pyramidal dressing of gauze. The iodoform roll and sutures are left in place for about ten days.

Grade 3 cysts should not be closed primarily, since this study shows a 53 per cent failure in cases so treated. Some form of partial closure, such as the MacFee operation, is recommended, inasmuch as the period of hospitalization is shorter, the local condition of the scar is better and the possibility of success is greater with partial closure than with the excision and open-packing operation. Since

it has become the policy of our services to close primarily only Grade 1 and Grade 2 cysts and to close partially all Grade 3 cysts, the average time of hospitalization has continued to fall.

It is recommended that the frankly septic cases be prepared preoperatively by hot sitz baths and local packs. Preoperative sulfonamides may be used by mouth, sulfanilamide may be dusted in locally at operation, and sulfadiazine may be given by mouth postoperatively.

To become proficient in preoperative grading, the surgeon should check his clinical grading of cysts with the report of the pathologist on the sectioned specimen. In addition, a careful history and physical examination are essential for proper grading; of these, the latter is the more important.

In this series of 128 cases that were operated on, the average hospital stay for all grades from date of operation to complete healing and return to duty was thirty-five days.

On this service the greatest problem in the care of pilonidal cystectomy applies to the excised cyst that has been left open and that heals with resulting excess scar formation. This scar mass tends to break down following trauma and superficial infection, resulting in shallow ulcers that are surrounded by dense fibrous tissue and are slow to heal. The plan adopted in such cases is bed rest, warm antiseptic packs and rigid aseptic technic in handling the dressing until healing is complete. The patient is then educated in the hygienic care and protection of the area before he is sent back to duty.

SUMMARY

It has been the purpose of this analysis to call attention to a method of preoperative grading of pilonidal cysts that has been helpful in determining those cases in which primary closure can be accomplished with a reasonable degree of success. No attempt has been made to bring forward any new type of operation, and all cases were treated by methods that up to this time have been accepted as being surgically sound.

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THE USE OF GAUZE INOCULATED WITH *PENICILLIUM NOTATUM* OR IMPREGNATED WITH CRUDE PENICILLIN IN THE TREATMENT OF SURFACE INFECTIONS*

R. S. MYERS, M.D.,† R. H. ALDRICH, M.D., R. W. HOWARD, M.D.,‡ AND R. A. WALSH, B.S.§

BOSTON

RECENT reports indicate that topically applied penicillin solutions and creams are effective in controlling surface infections.¹ There have also been articles suggesting that gauze dressings inoculated with *Penicillium notatum* or impregnated with the crude penicillin have a similar effect. Robinson and Wallace² have described a method by which they believe that mold-inoculated dressings can be readily prepared by the physician. They noted subsidence of infection and relief from pain in patients with staphylococcal infections treated by this type of dressing. Hobson and Galloway³ report 10 cases (burns, lacerations, ulcers and infected sloughing wounds) in which gauze dressings moistened with the crude penicillin produced by *P. notatum* cultures were used. They prevented infection in 3 cases and helped to subdue and control it in 7. Fisher⁴ obtained encouraging results from using crude penicillin locally, but noted that it had distinct limitations. He believes that to be effective the dressings should be applied every two or three hours, that crude penicillin, like purified penicillin, is ineffective against certain organisms, and that it is less effective against long-standing infections than against those of brief duration. He noted no toxic effects when the crude penicillin was used either locally or parenterally.

The present clinical study was undertaken to evaluate the use of *P. notatum*-inoculated gauze dressings made according to the method described by Robinson and Wallace. Some of the cases were subsequently treated with dressings impregnated with crude penicillin. Bacteriologic studies were made to determine the bacteriostatic and bactericidal effects of each lot of mold or liquor.

Preparation of Gauze and of Crude Penicillin

Pieces of 28-by-24-mesh absorbent gauze were folded to form eight thicknesses, cut circularly, placed in clean Petri dishes and sterilized in a hot-air oven for one hour at a temperature of 400°F. Five hundred cubic centimeters of distilled water was next placed in an Erlenmeyer flask, to which

was added 6 gm. of dehydrated yeast and 12 cc. of glycerin. Finally, a separate mixture of 12 gm. of lactose, 12 gm. of cornstarch and 30

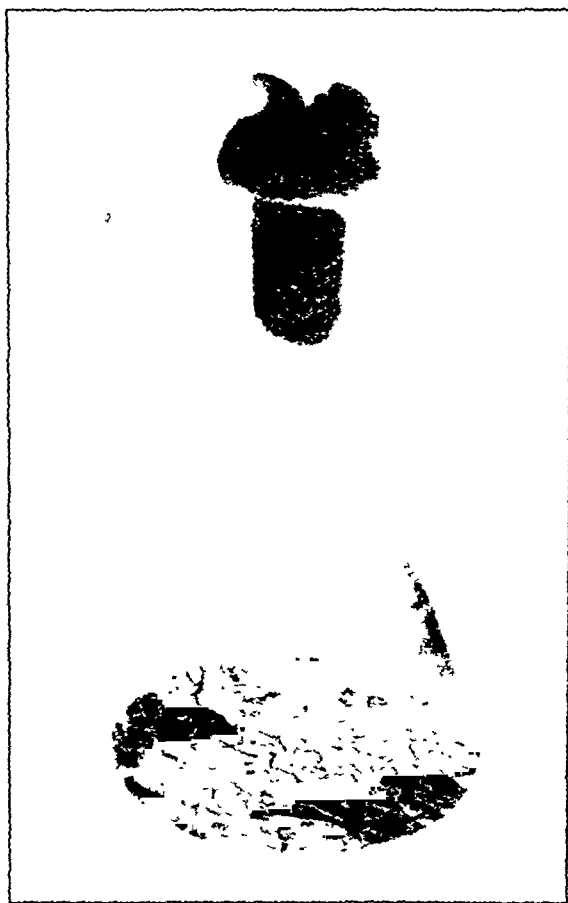


FIGURE 1. The *Penicillium notatum* Growing in an Erlenmeyer Flask.

The penicillin is secreted on the underside of the mold.

cc. of cold distilled water was added. The contents of the flask was stirred well and boiled for twenty minutes over a low flame. The Petri dishes and culture medium were cooled, and about 60 cc. of the medium was poured into each dish. A bit of the stock culture of *P. notatum* was then transferred to the plate with a flamed platinum loop. The dishes were placed in an incubator at a temperature of 23°C. The penicillin secreted during the growth process was deposited on the under-

*From the Surgical Section, Peter Bent Brigham Hospital, and the Department of Surgery for Surgical Research and Biology Department. This study was made in Boston.

†Attending surgeon, Harvard Medical School; associate in surgery, Peter Bent Brigham Hospital.

‡Assistant in surgery, Harvard Medical School; junior associate in surgery, Peter Bent Brigham Hospital.

§Attending physician in biology and pharmacology, Massachusetts College of Pharmacy.

†The stock culture was obtained through the courtesy of Charles Pfizer and Company, Brooklyn, New York. It was grown on Sabouraud's dextrose agar, and transfers were made at ten-day intervals to maintain a prolific strain.

surface of the gauze. Its concentration reached a maximum in twelve days and then rapidly retrogressed.

The medium used for the production of crude penicillin was a combination of 96 per cent nutrient broth and 4 per cent corn-steep liquor.* This was placed in flasks, which were sterilized by autoclaving, inoculated with *P. notatum* and incubated for about seven days at 23°C. The liquor, which was partially purified by filtration through a

cultures were made. Contaminated plates and flasks were discarded.

Method of Applying Dressings

Before the dressings were applied the lesions were prepared by cleansing with an aqueous cationic detergent or with hydrogen peroxide. Gauze pads inoculated with mold or impregnated with crude penicillin liquor were then applied and held in place by adhesive tape or bandage. Several cases

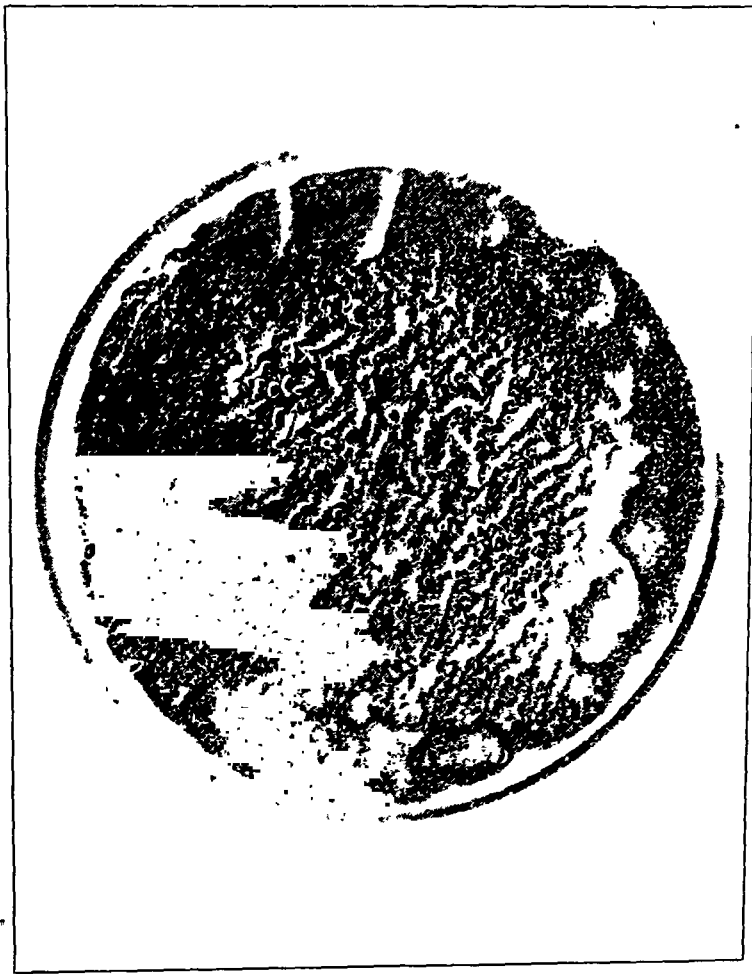


FIGURE 2. Gauze Inoculated with *Penicillium Notatum* in a Petri Dish.

Seitz filter, yielded a high titer of penicillin when assayed by the Oxford method.

The plates containing the impregnated gauze maintained their potency for about two weeks when kept at a temperature of 5°C. or lower, and the crude penicillin liquor could be kept for about four weeks at a temperature of 5°C. without any appreciable loss in titer.

All cultures were examined microscopically for bacterial contamination, and when necessary, sub-

of uterine cervicitis were also treated. In these, a pad of the mold-inoculated gauze or of gauze impregnated with crude penicillin was applied directly to the cervix. The dressing was held in place by a vaginal tampon for a period of thirty-six hours. Except for those on the uterine cervix, the dressings were renewed at intervals varying from one to four days. All the patients were ambulatory, thus making it difficult to change the dressings more frequently.

Types of Lesions Treated

Thirty-three patients with ulcers of the lower leg or ankle of one week to twenty years' duration were

*Corn-steep liquor is a by-product in the corn-refining industry and is obtainable from the Corn Products Sales Company, New York, New York.

treated for periods varying from two weeks to three and a half months. There were also 5 patients with chronic uterine cervicitis, 2 with postoperative lacerated-sinus wounds, 2 with breast wounds following radical mastectomy, in which there was necrosis of the skin and subsequent secondary infection, 2 with draining carbuncles, 1 with a small burn of the neck and secondary infection, 1 with a sloughing perineal wound and 1 with ulcerative stomatitis and secondary infection.

About half the cases were studied bacteriologically. Cultures were made before starting penicillin therapy and repeated during treatment. Most of them showed two or more types of organisms. Twenty-five cases exhibited *Staphylococcus aureus*.

Comment

The use of gauze inoculated with *P. notatum* or impregnated with crude penicillin was studied in 47 cases of surface infection. In view of the shortage of purified penicillin available for the treatment of surface infections, it was considered worth while to see whether such dressings could be conveniently prepared by the practicing physician. In our experience, homemade penicillin is much more difficult to prepare than is generally appreciated. Civilian physicians are advised to await a more plentiful supply of purified penicillin for the topical treatment of surface infections. Penicillin is too fickle a substance to be prepared by any except experienced hands. The parent mold is difficult to control, and



FIGURE 3. Application of a Mold-Inoculated Gauze Dressing.

11, *Staph. albus*, 5, beta-hemolytic streptococci, and 4, *Escherichia coli*. A few lesions showed *Proteus vulgaris*, *Bacillus subtilis* and diphtheroid bacilli. After treatment most of the affected surfaces continued to show the same organisms, but in fewer numbers.

In the majority of the cases previous treatment had been employed. Sulfonamide ointments, cationic germicidal solutions, chlorinated solutions and boric-acid ointment were among the substances used without noticeable beneficial effect.

Results

The results of treatment with *P. notatum*-inoculated gauze and crude-penicillin dressings are shown in Table 1.

a painstaking bacteriologic technic is required to avoid contamination.

Most of the cases treated in this series were mixed infections, showing more than one type of organism on culturing. The cases that had a pure culture of penicillin-sensitive organisms responded by healing. The cases that failed to heal continued to show the presence of the original infecting organisms, especially *E. coli*, *P. vulgaris* and *Staph. aureus* (a nonsusceptible strain).

Chronic or mixed infections did not respond so well as did acute infections. In the group of 33 patients with chronic ulcers of the lower extremities, many factors other than infection prevented healing. In this group, a different form of therapy intensively followed would probably have given equally good results.

The 13 cases listed as improved, although not entirely freed from the infecting bacteria, were noticeably better in that the wounds looked less angry, were drier and did not have the offensive odor that was usually present before treatment.

No local or systemic toxic effects were noted in

Chronic or mixed infections did not respond so well as did acute infections or those infected with but one strain of a penicillin-sensitive organism

Because of the difficulties associated with preparing crude penicillin and mold-inoculated gauze, physicians are advised to employ only purified

TABLE 1. Results of Treatment.

TYPE OF CASE	NO OF CASES	HEALED	IMPROVED	RESULT NO CHANGE	WORSE	NO FOLLOW-UP
Leg ulcer	33	14	10	6	1	2
Chronic endocervicitis	5	4	1	-	-	-
Pilonidal-sinus wound	2	1	1	-	-	-
Mastectomy wound	2	2	-	-	-	-
Carbuncle	2	2	-	-	-	-
Burn of neck	1	1	-	-	-	-
Peroneal wound	1	-	1	-	-	-
Ulcerative stomatitis	1	1	-	-	-	-
Totals	47	25	13	6	1	2

any of the patients treated by these methods. There was no evidence of sensitivity, and the patients reported the dressings to be comfortable.

penicillin for the treatment of cases of surface infection

SUMMARY

Forty-seven cases of surface infection were treated with *Penicillium notatum*-inoculated gauze dressings and crude penicillin. Twenty-five cases healed and 13 improved during treatment.

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MEDICAL PROGRESS

ENDOCRINE ASPECTS OF CANCER*

IRA T. NATHANSON, M.D †

BOSTON

THE earliest investigations concerning the relation of hormones to the genesis of tumors relied on indirect evidence. It was not until the isolation and identification of the action of certain of the sex hormones that the problem could be pursued on a more direct basis. Moreover, several of the synthetic carcinogenic hydrocarbons were found to have a basic chemical structure similar to cholesterol and to the hormones of the gonads and adrenal glands. Thus, experimental and clinical studies were further stimulated by the idea that atypical metabolism of the hormones might lead to oncogenesis. As a result of these observations, much information has been accumulated on the role of hormones in carcinogenesis. A symposium on the endocrinology of neoplastic disease was published in the July and August, 1944, issues of *Surgery*. The writer has drawn on these excellent articles,

as well as on other leading reviews, as one source of material. The present report summarizes and evaluates, so far as possible, some of the more significant experimental and clinical aspects of the relation of the hormones to carcinogenesis.

EXPERIMENTAL OBSERVATIONS

It is considered important in this review to cite the pertinent animal experiments so that they may be correlated, if possible, with clinical observations. Animals lend themselves readily to studies on cancer, since many develop spontaneous tumors that are similar to those in the human being. Therefore, the subject is reviewed from this standpoint, but it is necessary to stress that caution in interpretation is essential.

Tumors of Breast

Cancer of breast. The early observations of Tyzzer,¹ Slye² and others established the role of heredity in the development of tumors in mice. Later studies revealed that other factors were also involved.³ Thus, it was demonstrated that ovar-

*From the Medical Laboratories of the Collis P. Huntington Memorial Hospital, Harvard University, the Tumor Clinic of the Massachusetts General Hospital and the Pondville Hospital, Walpole, Massachusetts (Massachusetts Department of Public Health).

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†Instructor in surgery, Harvard Medical School, assistant in surgery, Massachusetts General Hospital, assistant surgeon, Pondville Hospital.

tomy caused a marked reduction in the incidence of spontaneous mammary cancer⁴ and delayed the appearance of those tumors which arose in female mice having a high susceptibility to the disease.^{5,6} The reduction in rate varied directly with the age of the mouse at castration, except in newborn mice; for example, the younger the age at ovariectomy, the lower the incidence of tumor. The incidence of breast tumors in mice spayed immediately after birth was higher than in mice castrated at maturity.⁷ It has been postulated that after castration in newborn mice the adrenal glands, which secrete steroid hormones, substitute for the ovaries, since mammary and uterine stimulation were noted and adrenocortical hyperplasia developed later in life.⁸ Mammary cancer was produced in the male mice of a highly susceptible strain by the transplantation of the ovaries of their sisters,⁹ and it was further noted that the incidence of tumors in the female could be reduced by the implantation of testes.¹⁰ Ordinarily, male mice do not develop cancer of the breast. It was also observed that the breast cancer rate was lower in virgin than in breeding females.¹⁰ Forced breeding increased the incidence of breast tumors over that of normally breeding mice.¹¹ Claims that abnormalities in the sexual cycle are a factor have not been proved.¹² All these experiments suggested the importance of the ovary in the production of such lesions.

After the identification of the estrogens, attempts to produce breast cancer with these hormones were not successful until 1932. Lacassagne¹³ was the first to report the appearance of breast cancer after the injection of estrogens in male mice of a strain in which the incidence was high in the female. It was not possible to initiate the disease in males belonging to a strain in which the incidence of mammary tumor was extremely low.¹⁴ Many others have since confirmed and extended these studies.^{15,16,17} The administration of estrogens of different chemical structure¹⁴ and synthetic estrogenic preparations, such as diethylstilbestrol^{18,19} and triphenylethylene,²⁰ which are not directly related to the natural compounds or hydrocarbon carcinogenic agents, produced the same effect. Thus, it appears that any compound with the same physiologic effect can elicit the disease and that it is not dependent on a specific chemical structure of the hormone.²¹

Recently, Bittner^{22,23} discovered that a third factor, present in the milk of high-tumor-strain mothers, was essential to the development of mammary cancer. The suckling of newborn females of a low tumor strain on high-tumor-strain mothers significantly increased the incidence of cancer of the breast. A reduction in rate was noted if the situation was reversed. Twombly²⁴ utilized this foster nursing technic and found that it was possible to initiate mammary cancer in male mice of a low tumor strain when they were injected with

estrogens. It has been maintained that the extent of response of breast tissue of nonsusceptible animals to estrogens is limited regardless of the duration or the amount of hormone administered. Factors that ordinarily govern cell growth may prevent further progression of cells to a malignant state. Defects in the governing mechanism may allow for neoplastic change, provided the cells are susceptible. Geschickter's^{25,26} reports are at variance with this point of view. Rats ordinarily have a low incidence of mammary cancer. He noted a high incidence of mammary cancer in the rat induced by the prolonged administration of estrogens to apparently nonsusceptible animals. Metastases were also observed. Noble, McEuen and Collip,²⁷ using essentially the same method in a different strain of rats, noted tumors that were extremely hyperplastic. The tumors were not considered to be malignant, even though they resembled the lesions described by Geschickter. Moreover, regressions occurred after removal of the hormonal stimulus.²⁸ If it is confirmed that mammary cancer can be produced in a species with a nontumor genetic constitution, the role of estrogens as etiologic factors may assume greater significance.

The incidence of breast cancer in mice can be increased by the transplantation of the anterior lobe of the hypophysis under conditions that make possible the long survival of the transplant. Loeb and Kirtz^{16,29} found that transplantation of the glands from several brothers to a sister in a high tumor strain appreciably raised the incidence of mammary cancer. This did not occur in the strains in which the susceptibility to tumor was slight. Moreover, cancer could not be induced in the female of the high tumor strain in the absence of the ovaries. Therefore, the increased incidence of cancer was presumably brought about by an increased estrogen production resulting from pituitary stimulation of the ovaries in the intact animal.

Attempts have been made to influence the incidence and course of spontaneous mammary cancer in mice by the administration of gonadotropins. Chorionic gonadotropins had no effect, regardless of the age of the animals at the onset of the experiment, even though there was pronounced enlargement of the ovaries.³⁰ Equine gonadotropin (pregnant mare's serum) and pituitary gonadotropin retarded the onset and decreased the incidence of the cancer in the virgin mouse when treatment was commenced at approximately one month of life.³¹ Administration of the same hormones commencing when the mice were seven months old (the early cancer age) increased ovarian size but did not appreciably alter the onset and course of the tumors.³² The decrease in incidence produced by these hormones in the young immature animal may be related to the formation of antihormones, which in time would result in ovarian and mammary atrophy.

Thyrotropic extracts have been reported to have an inhibitory effect on the development of mammary cancer,³³ but this has not been confirmed.³⁴ Hypophysectomy at an early age theoretically reduces the incidence of spontaneous mammary tumors in mice if the animal can be maintained. Gardner,³⁵ however, found that if mice bearing spontaneous tumors were hypophysectomized in the last half of pregnancy or post partum the tumors grew progressively and new tumors frequently appeared.

Nathanson and Andervont³⁶ and others^{12,37,38} have found that testosterone will significantly lower the incidence of spontaneous mammary cancer in a highly susceptible strain. This is presumably brought about by an antagonism to the estrogens or the inhibition of the pituitary gland, which results in ovarian atrophy, or both. Desoxycorticosterone acetate³⁹ and progesterone⁴⁰ have no influence on the incidence or course of spontaneous breast cancer. None of the hormones tested thus far^{12,36} or hypophysectomy³⁵ has any effect on the course of a tumor once it has developed. No significant difference in the excretion levels of estrogens and 17-ketosteroids has been found between strains with high and low rates of spontaneous mammary tumor.⁴¹

It is now agreed by most observers that at least three factors are necessary for the genesis of breast cancer in the mouse. These are a heredity factor, the presence of the ovaries or their secretion and the milk influence. All three must be present or cancer does not develop in the experimental animal.²³

Fibroadenomas of breast. Spontaneous mammary cancer in the rat is infrequent, but fibroadenoma is a relatively frequent disease. One strain, with a relatively high incidence of the tumors, exhibited prolongation of the estrous cycle and a deficiency in ovulation.⁴² The initiation of fibroadenomas was attributed to the unopposed action of the estrogens resulting from abnormalities in the sexual cycle. It has been reported that estrogens given over a long period of time produce a high percentage of true fibroadenomas in a strain of rats that ordinarily have a low spontaneous incidence.²⁶ Others have been unable to confirm this, but the techniques were not identical.⁴³ Studies relative to hormonal influences on the histologic appearance of the tumors are more conclusive. Estrogens stimulate the epithelial elements of early spontaneous, autotransplanted or homotransplanted fibroadenomas and produce adenomas and cystadenomas.⁴⁴ Androgens^{44,45} and progesterone,⁴⁶ on the other hand, inhibit the epithelial component and produce fibrosis. Prolonged administration of estrogens revealed foci of abnormal proliferation of the epithelium in the tumors, which in some cases resembled cancer.⁴⁷ Thus it can be seen that in contrast to true cancer, the course and histologic appearance of benign tumors can be altered by hormones.

Tumors of Uterus

Cancer of cervix. Overholser and Allen⁴⁸ in 1931 reported the production of a lesion in the cervix in the monkey following estrogen injection that they believed to be carcinoma. Later studies by them⁴⁹ and by others^{50,51} revealed that the lesion was actually squamous metaplasia. This type of lesion was shown to regress after such a stimulus was removed or when progestin was given with the estrogen.⁵ Nevertheless, in 1936 several investigators described the appearance of a carcinoma-like lesion in the cervix of the mouse after estrogen was administered.^{52,53} This was of great interest, since cervical cancer does not develop spontaneously in the mouse. Subsequently, the production of cancer of the cervix and vagina after estrogen administration in the mouse has intensively been studied.^{12,54-56} The lesions are of the squamous-cell type since the mouse has no mucous glands in the cervix.⁵⁷ Early experiments were done in mice that were susceptible to mammary cancer. These studies were complicated by the fact that breast lesions developed before cervical lesions. It was therefore essential to remove the breast cancers as they arose.⁵⁴ This pitfall was overcome when it was noted that estrogens could induce cancer in strains of mice that were resistant to mammary cancer.⁵⁷ Hence, in contrast to the strain specificity necessary in the development of cancer of the breast in the mouse, the neoplastic response of the cervix to estrogens was not particularly governed by this characteristic. Consequently, there was scant evidence to prove a hereditary influence. Simultaneous administration of androgens or of progestin to any strain of mice did not alter the incidence of cervical cancer.⁵⁷ It was also established that the milk influence was not necessary.⁵⁷ Since there might be considerable doubt regarding the histologic diagnosis of cancer, several investigators proved the autonomy of the lesion by successful transplantation into other animals of the same strain.⁵⁴

Cancer and hyperplasia of endometrium. Estrogens can produce typical hyperplasia of the endometrium in animals.⁵⁸ If treatment is commenced before puberty or is prolonged, squamous metaplasia of the epithelium of the endometrium may occur.⁵⁹ Estrogens frequently produce pyometra,^{15,60} and some believe that this is the cause of the hyperplasia.⁶¹ Cystic hyperplasia in rabbits,⁶² guinea pigs⁶³ and monkeys⁶⁴ similar to that seen in the human female has been observed following prolonged treatment with estrogens. Hypophysectomy increases the susceptibility to the production of endometrial metaplasia not only with estrogens but also with androgens and progestin.⁶⁵ Hyperplasia and atypical proliferation of the endometrium follows partial ovariectomy in the guinea pig.⁶⁶ Irradiation of the ovaries in the guinea pig⁶⁷ and implantation of testicular tissue in mice⁶⁸ also result in endometrial

and a progressive erosion of the corpus is suggested by the fact that hyperplasticity induced in the experimental animals by the administration of the oestrogens are not re-inhibited by oestrogens if given simultaneously.¹¹ There is erosion of the uterus and the cervical and production of cancer of the endometrium. This is of interest because the rat is usually susceptible to oestrogen in cancer.¹² Gould¹³ found that spontaneous activity in the rabbit's endometrium. The rabbit was said to be oestrogenic, arose in the uterus of relatively old animals and gland atrophy and metastasis. Changes in those caused by oestrogens were found in rats. These oestrogens occurred frequently in the endometrium of pregnancy, which is produced after damage and hence an oestrogenic effect.

Uterus. Numerous attempts to induce cancer of the uterus in species such as mice, rabbits have been without success. The rat is especially susceptible so that these may be induced simply by the injection of oestrogens.¹⁴ The tumors arise usually between the myometrium but sometimes between the uterus thus covering hemithyphal. It appears throughout the abdominal cavity.¹⁵ Many are subperitoneal, and a large number of malignant epithelial carcinomas are found in the peritoneal fluid or ascitic endometrium.¹⁶ They occur in relation to the mechanism of the end system. Some of the lesions are considered malignant since they involve adjacent structures like the pancreas, liver and abdominal cavity and are not uncommonly because regression when treatment is discontinued.¹⁷ Another to another animal is unsuccessful. It has been injected with oestrogens.¹⁸ If one or two oestrogens¹⁹ or oestrogenic hormones²⁰ is injected simultaneously with the oestrogenic hormone. The induction system in the uterus pig is therefore a good one for studies susceptibility to tumor formation.

Primary Ovary

Primary tumors of the hypophysis seldom occur in rats. In 1950 three groups of rats²¹ reported hyperplasia of the pituitary and the formation of chromophobe adenomas and also of both sexes after treatment with oestrogens. These adenomas may be found in other animals of the same strain, but when the dose is treated with oestrogen.²² The adenomas of the intermediate lobe of the pituitary have also been observed after oestrogen.²³ These tumors change to car-

cinoma in all species of the same species, which demonstrates again the importance of a specific susceptibility to tumor formation. A more detailed review of the subject was recently written by Selby.²⁴

Primary of Ovary

Tumors of the ovary of the rat have appeared after the injection of the oestrogens.²⁵ In most cases the tumors arise in the ovary when spermatogenesis begins, but tumors have likewise been produced in the ovary when extracts of the anterior pituitary gland of sheep were injected in combination with oestrogen.²⁶ It has been suggested that the tumors arise from the primary germ cells as a result of stimulation of the gonocytes by gonadotropic hormones.²⁷ Seminomas have appeared after gonadotropin²⁸ in which case as the gland regressed, the spermatogenesis went on to tumor formation instead of undergoing normal differentiation. This effect was ascribed to excessive secretion of the gonadotropic hormones as a result of the partial castration, a state that may also arise after oestrogen produced by the oestrogenic injections. Although the evidence is not conclusive for a hormonal origin, there appears to be a common denominator. All three methods of tumor production, apparently, are related to increased stimulation of the gonads by the gonadotropins.

The production of interstitial cell tumors of the ovary in certain strains of mice by the injection of oestrogens²⁹⁻³¹ suggests a more definite hormonal relation. Simultaneous injection of testosterone or a certain dose level does not prevent the appearance of tumors but the rate of change is retarded.³² In the sequence of events leading up to the development of these tumors progressive phases of atypical cells appear with atrophy of the tubules. This is manifested by the formation of three generations of Leydig cells. Tumors may arise from any one generation or from a combination of two or of all three generations of cells.³³ These tumors appear malignant and metastasize widely, particularly to the lymph nodes.³⁴ Transplantation to other animals is successful when the host is treated with oestrogen.³⁵ Long-protracted injections of equine gonadotropins elicited changes in the ovary of certain mice that resembled those seen in the early stages of the tumors developed by oestrogens.³⁶ Thus as in the case of the first tumors, the gonadotropic hormones may be responsible for the changes. Many of the tumors appear to function since the seminal vesicles and prostate of the animals exhibited an androgen effect.³⁷ Tumors of this type produced by any form of oestrogen appear to be species limited as well as strain limited. Like cancer of the mammary gland and cervix in the mouse, the tumors arise only after prolonged treatment and after the tissue fails to respond in the usual fashion, or has regressed.³⁸

Thyrotropic extracts have been reported to have an inhibitory effect on the development of mammary cancer,³³ but this has not been confirmed.³⁴ Hypophysectomy at an early age theoretically reduces the incidence of spontaneous mammary tumors in mice if the animal can be maintained. Gardner,³⁵ however, found that if mice bearing spontaneous tumors were hypophysectomized in the last half of pregnancy or post partum the tumors grew progressively and new tumors frequently appeared.

Nathanson and Andervont³⁶ and others^{12,37,38} have found that testosterone will significantly lower the incidence of spontaneous mammary cancer in a highly susceptible strain. This is presumably brought about by an antagonism to the estrogens or the inhibition of the pituitary gland, which results in ovarian atrophy, or both. Desoxycorticosterone acetate³⁹ and progesterone⁴⁰ have no influence on the incidence or course of spontaneous breast cancer. None of the hormones tested thus far^{12,36} or hypophysectomy³⁵ has any effect on the course of a tumor once it has developed. No significant difference in the excretion levels of estrogens and 17-ketosteroids has been found between strains with high and low rates of spontaneous mammary tumor.⁴¹

It is now agreed by most observers that at least three factors are necessary for the genesis of breast cancer in the mouse. These are a heredity factor, the presence of the ovaries or their secretion and the milk influence. All three must be present or cancer does not develop in the experimental animal.²³

Fibroadenomas of breast. Spontaneous mammary cancer in the rat is infrequent, but fibroadenoma is a relatively frequent disease. One strain, with a relatively high incidence of the tumors, exhibited prolongation of the estrous cycle and a deficiency in ovulation.⁴² The initiation of fibroadenomas was attributed to the unopposed action of the estrogens resulting from abnormalities in the sexual cycle. It has been reported that estrogens given over a long period of time produce a high percentage of true fibroadenomas in a strain of rats that ordinarily have a low spontaneous incidence.²⁶ Others have been unable to confirm this, but the technics were not identical.⁴³ Studies relative to hormonal influences on the histologic appearance of the tumors are more conclusive. Estrogens stimulate the epithelial elements of early spontaneous, autotransplanted or homotransplanted fibroadenomas and produce adenomas and cystadenomas.⁴⁴ Androgens^{44,45} and progesterone,⁴⁶ on the other hand, inhibit the epithelial component and produce fibrosis. Prolonged administration of estrogens revealed foci of abnormal proliferation of the epithelium in the tumors, which in some cases resembled cancer.⁴⁷ Thus it can be seen that in contrast to true cancer, the course and histologic appearance of benign tumors can be altered by hormones.

Tumors of Uterus

Cancer of cervix. Overholser and Allen⁴⁸ in 1933 reported the production of a lesion in the cervix of the monkey following estrogen injection that they believed to be carcinoma. Later studies by them⁴⁹ and by others^{50,51} revealed that the lesion was actually squamous metaplasia. This type of lesion was shown to regress after such a stimulus was removed or when progestin was given with the estrogen. Nevertheless, in 1936 several investigators described the appearance of a carcinoma-like lesion in the cervix of the mouse after estrogen was administered.^{52,53} This was of great interest, since cervical cancer does not develop spontaneously in the mouse. Subsequently, the production of cancer of the cervix and vagina after estrogen administration in the mouse has intensively been studied.^{12,54-56} The lesions are of the squamous-cell type since the mouse has no mucous glands in the cervix.⁵⁷ Early experiments were done in mice that were susceptible to mammary cancer. These studies were complicated by the fact that breast lesions developed before cervical lesions. It was therefore essential to remove the breast cancers as they arose.⁵⁴ This pitfall was overcome when it was noted that estrogens could induce cancer in strains of mice that were resistant to mammary cancer.⁵⁷ Hence, in contrast to the strain specificity necessary in the development of cancer of the breast in the mouse, the neoplastic response of the cervix to estrogens was not particularly governed by this characteristic. Consequently, there was scant evidence to prove a hereditary influence. Simultaneous administration of androgens or of progestin to any strain of mice did not alter the incidence of cervical cancer.⁵⁷ It was also established that the milk influence was not necessary.⁵⁷ Since there might be considerable doubt regarding the histologic diagnosis of cancer, several investigators proved the autonomy of the lesion by successful transplantation into other animals of the same strain.⁵⁴

Cancer and hyperplasia of endometrium. Estrogens can produce typical hyperplasia of the endometrium in animals.⁵⁸ If treatment is commenced before puberty or is prolonged, squamous metaplasia of the epithelium of the endometrium may occur.⁵⁹ Estrogens frequently produce pyometra,^{15,60} and some believe that this is the cause of the hyperplasia.⁶¹ Cystic hyperplasia in rabbits,⁶² guinea pigs⁶³ and monkeys⁶⁴ similar to that seen in the human female has been observed following prolonged treatment with estrogens. Hypophysectomy increases the susceptibility to the production of endometrial metaplasia not only with estrogens but also with androgens and progestin.⁶⁵ Hyperplasia and atypical proliferation of the endometrium follows partial ovariectomy in the guinea pig.⁶⁶ Irradiation of the ovaries in the guinea pig⁶⁷ and implantation of testicular tissue in mice⁶⁸ also result in endometrial

erplasia. A protective action of the corpus uterini is suggested by the fact that hyperplasia is easily induced in the experimental animal by injection of estrogens if the ovaries are not removed⁶⁹ or if progesterone is given simultaneously.⁷⁰ In contrast to cancer of the breast and the cervix, experimental production of cancer of the endometrium is rare. This is of interest because the endometrium is usually susceptible to estrogen stimulation. Greene⁷¹ found that spontaneous tumors develop in the rabbit's endometrium. The tumors, which were said to be adenomas, arose in the glandular mucosa of relatively old animals and spread by local extension and metastasis. Changes similar to those caused by estrogens were found in other organs. These adenomas occurred frequently in animals that had toxemia of pregnancy, which may have produced liver damage and hence an inability to inactivate the estrogens.

Uterine Myomas. Numerous attempts to induce myomas of the uterus in species such as mice, rats, and rabbits have been without success. The guinea pig is singularly susceptible so that these tumors may be induced simply by the injection of estrogenic hormones.⁷²⁻⁷⁴ The tumors arise usually in the subserosa and the myometrium but sometimes involve the mucosa, thus causing hemorrhage. They may appear throughout the abdominal cavity in both sexes.^{73,75} Many are subperitoneal, and although the site of origin is not definitely established, the earliest lesions are found in the peritoneal omentum⁷⁶ or celomic endothelium.⁷⁷ They are thought to occur in relation to the mesenteries of the stomach and spleen. Some of the lesions are considered to be malignant since they involve adjacent structures, such as the pancreas, liver and abdominal wall. The lesions are not autonomous because regression occurs when treatment is discontinued.^{72,75} Transplantation to another animal is unsuccessful unless the host is injected with estrogens.⁷⁷ If progesterone or testosterone⁷⁸ or desoxycorticosterone acetate⁷⁹ is injected simultaneously with the estrogens, the tumors fail to appear. The initiation of uterine myomas in the guinea pig is therefore a good example of a species susceptibility to tumor formation.

Tumors of Pituitary Gland

Spontaneous tumors of the hypophysis seldom occur in mice or rats. In 1936, three groups of investigators⁸⁰⁻⁸² reported hypertrophy of the pituitary gland and the formation of chromophobe adenomas in mice and rats of both sexes after continued treatment with estrogens. These adenomas may be transplanted to other animals of the same strain, particularly when the host is treated with estrogen.⁸² Transplanted adenomas of the intermediate lobe of the pituitary gland in rats have also been observed after estrogen therapy.⁸³ These various changes do not

occur in all strains of the same species, which demonstrates again the importance of a specific susceptibility to tumor formation. A more detailed review of the subject was recently written by Selye.⁸⁴

Tumors of Testis

Teratomas of the testes of the fowl have appeared after the injection of zinc chloride.⁸⁵ In most cases the tumors arose in the spring when spermatogenesis begins, but tumors have likewise been produced in the summer when extracts of the anterior pituitary gland of sheep were injected in combination with zinc chloride.⁸⁶ It has been postulated that the tumors arise from the primary germ cells as a result of stimulation of the gonocytes by gonadotropic hormones.⁸⁷ Seminomas have appeared after partial gonadectomy,⁸⁸ in which case, as the gland regenerated, the spermatogonia went on to tumor formation instead of undergoing normal differentiation. This effect was ascribed to excessive secretion of the gonadotropic hormones as a result of the partial castration, a state that may also arise after necrosis produced by zinc chloride injections. Although the evidence is not conclusive for a hormonal origin, there appears to be a common denominator. All three methods of tumor production, apparently, are related to increased stimulation of the gonads by the gonadotropins.

The production of interstitial cell tumors of the testes in certain strains of mice by the injection of estrogens⁸⁹⁻⁹¹ suggests a more definite hormonal relation. Simultaneous injection of testosterone at a certain dose level does not prevent the appearance of tumors, but the rate of change is retarded.⁹² In the sequence of events leading up to the development of these tumors, progressive phases of atypical cells appear with atrophy of the tubules. This is manifested by the formation of three generations of Leydig cells. Tumors may arise from any one generation or from a combination of two or of all three generations of cells.⁹² These tumors appear malignant and metastasize widely, particularly to the lymph nodes.⁹⁰ Transplantation to other animals is successful when the host is treated with estrogen.⁹² Long-continued injections of equine gonadotropins elicited changes in the testes of certain mice that resembled those seen in the early stages of the tumors developed by estrogens.⁹³ Thus, as in the case of the fowl tumors, the gonadotropic hormones may be responsible for the changes. Many of the tumors appear to function, since the seminal vesicles and prostate of the animals exhibited an androgen effect.⁹⁰ Tumors of this type produced by any form of estrogen appear to be species limited as well as strain limited. Like cancer of the mammary gland and cervix in the mouse, the tumors arise only after prolonged treatment and after the tissue fails to respond in the usual fashion, or has regressed.¹²

Tumors of Adrenal Gland

Tumors of the adrenal gland in mice are exceedingly rare, but a technic devised by Woolley, Fekete and Little^{7,8,94} has resulted in the production of many of these lesions. A variety of changes appear in these glands subsequent to castration in both sexes during the first days of life. The development of the different types of lesions depends to a great degree on the strain used. In one strain, slight hyperplasia occurs, whereas in another, all the mice develop adrenal hyperplasia, nodular or diffuse, which is accompanied by feminization of both sexes.⁸ Cancer of the breast may occur in these animals, presumably as a result of estrogenic substances secreted by the adrenal glands. All the animals of a third strain develop adrenocortical carcinoma at about one year of age.⁹⁵ Early in the development of the process, before true carcinoma appears, there may be an accompanying feminization, but masculinization appears with the onset of carcinoma. The tumors originate in the outer zones of the cortex, and the transitions from hyperplasia to carcinoma and from a feminization to masculinization can be easily followed.⁹⁵ Studies of the excretion of estrogenic hormone in the urine of mice with adrenal hyperplasia reveal about six times as much as is found in control animals.⁹⁶

Lymphoid Tumors

Lymphoid tumors and leukemia arise spontaneously in some strains of mice and rats, and in general there is a higher incidence in the male. Injection of estrogens into any strain of mice that has a tendency to develop these lesions results in an increased incidence of the diseases,⁹⁷⁻⁹⁹ and the incidence can also be raised by treatment with carcinogenic agents or x-ray.^{100,101} As in mammary carcinoma, the milk influence seems to be necessary in the genesis of these lesions.¹⁰² The lesions are usually widespread and can be easily transplanted. Murphy and Sturm¹⁰³ reported that removal of the adrenal glands greatly increases the susceptibility of rats to a transplanted lymphatic leukemia. They also found that the injection of adrenotropic hormone, adrenocortical extract and desoxycorticosterone acetate effectively reduced the percentage of "takes" of transplanted leukemic tissue.¹⁰⁴ No effect could be demonstrated on the eventual progress of the disease if the transplants were successful. Castration of the male in one strain of mice increased the incidence of the leukemia to that of the untreated female. Ovariectomy in the female in the same strain had no effect on the incidence of leukemia. Injection of testosterone in the ovariectomized female reduced the incidence to that of the untreated males.¹⁰⁵ In another study the incidence of leukemia in the female was reduced after ovariectomy but orchidectomy in the male had no effect.¹⁰⁶ Although there is some difference between these two studies, the age at castration

may have been a factor. Heilman and Endel¹⁰⁷ noted temporary retardation of the growth of transplanted leukemia after the administration of Compound E. After a time, however, the lesions became refractory and resulted in the death of the animal.

Tumors of Prostate Gland

Enlargement of the prostate gland occurs in about 80 per cent of dogs above the age of about 8 years.¹⁰⁸ Huggins and his collaborators¹⁰⁹ demonstrated that androgens given to the dog increased prostatic secretion and produced hyperplasia of the epithelial cells. Metaplasia occurred in some animals, and simulated the histologic appearance of cancer. Castration or injection of estrogens caused regression of the metaplasia and inhibited the production of prostatic fluid. Estrogens in themselves produce enlargement of the prostatic gland in the dog, which regresses when treatment is discontinued. On the other hand, continuous injection over a long period brings about squamous metaplasia of part of the epithelium of the prostate gland of the mouse.^{110,111,112} A similar change can be effected in the rhesus monkey.^{113,114} The atypical effects do not occur when testosterone or progesterone is injected simultaneously with estrogens.^{115,116} In rabbits, estrogen injection causes squamous metaplasia of the urethra around the orifice of the seminal vesicle.¹⁰⁸ Estrogens also cause hypertrophy of the seminal vesicles of mice. In no species of animal, however, has carcinoma of the prostate been produced by the administration of either androgen or estrogen. This is of interest in light of the recent observations regarding the relation of these hormones to cancer of the prostate in man. It appears that both hormones act on the prostate gland but in an entirely different fashion.

Other Tumors

Spindle-cell sarcomas have been reported in mice and rats at the site of injection of estrogens in oil.¹¹⁷ These have also appeared, however, after the injection of other substances other than estrogens that were dissolved in oil.¹¹⁸ They have not been observed when pellets of estrogens have been implanted.¹¹⁹ Osteogenic tumors have been reported as occurring in one strain of mice.¹¹⁹ Both osteosarcoma and osteogenic sarcomas were observed and were frequently multiple.¹²⁰ Approximately 75 per cent of the females and 25 per cent of the males develop these lesions on an average of one and a half years of age, the females developing the tumors somewhat earlier than the males.¹¹⁹ Injections of estrogens increased the incidence in males and decreased the age at which the tumors appeared in both sexes.¹²¹

Summary

A wide variety of tumors can be produced and altered in the experimental animal, but these a

endent on the species, the strain and the individual susceptibility of the animal and there seems to be some limiting factor in the proportion of tumors in animals in which attempts have been unsuccessful. Consequently, it is difficult to translate these observations to the study of human cancer. They are, however, of great importance as a tool in the study of oncogenesis in general.

(To be concluded)

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SE RECORDS OF THE SSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30491

PRESENTATION OF CASE

An eighteen-year-old-girl, a student, was admitted to the hospital with diarrhea.

Nine years prior to admission, at the age of nine, the patient first noted mild diarrhea with two to three soft stools a day. This gradually grew worse over a period of years until two and a half years before entry, at which time she had a sudden increase in the diarrhea, with many watery stools daily, which never contained blood. This was associated with anorexia, nausea, vomiting, discomfort in the right upper quadrant, generalized malaise and some fever. These symptoms were presently followed by deep jaundice. She was treated at a local hospital, where a diagnosis of catarrhal jaundice was made. She remained in the hospital several weeks, and the jaundice disappeared. Following this episode she had a partial remission of diarrhea for about a year. One and a half years prior to admission she developed nasal catarrh associated with fever. During this episode the diarrhea became worse and some blood streaking in the stools was noted; there was no jaundice. The diarrhea showed several remissions and exacerbations, with frequent blood streaking. About five months before admission, a small amount of sugar was found in the urine, and a physician placed her on a strict diabetic diet without insulin. No blood sugar determinations were done at that time. She had considerable anorexia and lost about 35 pounds in four months. The diarrhea continued and was associated with marked tenesmus. Two weeks prior to entry a blood sugar was done at another hospital and was found to be 80 mg. per 100 cc. Because of the persistent diarrhea, an ileostomy was recommended. Five days before entrance into this hospital the diarrhea increased, there being fifteen to twenty watery stools daily, with some blood clots. She developed fatigue, lassitude, drowsiness and a craving for salt and water.

The past history was noncontributory. The patient's mother and her grandfather, aunt and uncle on her mother's side all had diabetes mellitus.

*On leave of absence.

Physical examination revealed a pale, emaciated young girl appearing acutely ill and dehydrated. There was marked clubbing of the fingers. The heart appeared slightly enlarged to the left, and there was a soft blowing systolic murmur over the pulmonic area, which disappeared on inspiration. The abdomen was tender, without spasm. A definitely spastic colon was palpable.

The temperature was 101.4°F., the pulse 136, and the respirations 24. The blood pressure was 120 systolic, 55 diastolic.

Examination of the blood showed a red-cell count of 3,550,000, with 10 gm. of hemoglobin. The white-cell count was 8400, with 73 per cent neutrophils, 26 per cent lymphocytes and 1 per cent monocytes. A catheterized urine specimen had a specific gravity of 1.018, with no albumin or sugar; a few white cells were seen in the sediment. The stool was grossly bloody, with clots. The blood sugar was 95 mg. per 100 cc. The serum nonprotein nitrogen was 23 mg. per 100 cc., the chloride 94 milliequiv. per liter, and the protein 4.95 gm. per 100 cc., with an albumin-globulin ratio of 0.93. The prothrombin time was 33 seconds (normal, 18 to 20 seconds). A urine culture was sterile. A blood Hinton test was negative.

Röntgenograms of the chest and abdomen revealed only some increase in lung markings and a diffuse haziness of the abdomen, suggesting an accumulation of fluid.

The patient's temperature ranged between 100 and 102°F. There was apparently some transient jaundice on the first hospital day, but none thereafter. She was given numerous transfusions of whole blood and plasma, together with intravenous saline solution, Amigen and vitamins, as well as sulfadiazine. On the second hospital day, following a plasma infusion, she developed a chill, with a rise in temperature to 103.6°F. and some vomiting. A blood culture taken at the time was negative. On the following day marked ankle edema was noted, together with basal rales. The serum protein at that time was 4.4 gm. per 100 cc., with a chloride of 92 milliequiv. and a sodium of 128.3 milliequiv. per liter. On the seventh hospital day, proctoscopy revealed an extremely friable bleeding mucosa with a granular and edematous appearance but no frank ulceration. This was thought to be compatible with an acute ulcerative colitis. A stool smear showed no cysts, and there were many red and white cells present. The following day an ileostomy was performed, and examination of a small piece of ileum revealed acute and chronic inflammation with ulceration. At the time of operation about a liter of ascitic fluid was removed.

Following the operation, the temperature rose to 104.5°F., and the edema increased, with distended neck veins, a rapid pulse and slow gasping respirations. The heart was found to be enlarged to the left, and there were moist rales at the bases of the

lungs. At that time the serum protein was 4.97 gm. per 100 cc., with an albumin-globulin ratio of 0.8; the chloride was 91.4 milliequiv. per liter, the prothrombin time 44 seconds (normal, 18 to 20 seconds) and the van den Bergh 3.3 mg. direct, and 8.4 mg. indirect.

The patient was given oxygen and digitalized. She was also given 25 per cent albumin intravenously, as well as plasma and whole blood. She was disoriented, was only slightly responsive and developed a high-pitched cry. No reflexes could be obtained in either the upper or lower extremities. The patient rallied somewhat following the intravenous therapy, the edema decreased, and she became more responsive. On the tenth hospital day aspiration of the stomach by a Levine tube revealed dark-brown fluid that gave a ++ guaiac reaction. The following day the patient suddenly became pulseless and expired.

DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: We are presented with a diagnosis of what was wrong with this patient. It says in the abstract that the patient had acute ulcerative colitis. At operation the surgeon removed a bit of ileum, which was said to show acute and chronic inflammation with ulceration. So as a starting point I think that we have to accept the fact that this patient had colitis and ileitis. But the problem is to explain why an eighteen-year-old girl should have had diarrhea for nine years and then die of the diarrhea. I do not believe that she had only ulcerative colitis and ileitis. There must have been a more deep-seated disease to explain this picture. In the analysis of the situation it comes down to a discussion of what causes prolonged diarrhea in young people.

First we have to consider that this might have been gastrogenous in origin. There is no statement concerning the results of a gastric analysis, but I cannot conceive that lack of hydrochloric acid could have explained this situation, although we know that in old people achlorhydria can cause prolonged diarrhea.

In regard to the colon, we are presented with a statement that she had ulcerative colitis, and although I think that this was not true idiopathic ulcerative colitis, we are not favored with reports of x-ray examination of the bowel to see whether ulcerations were present.

I see Dr. Logan Roots, of China, in the audience; he might suggest that this sounds almost like cholera. There are certain symptoms, such as the craving for salt and water, that suggest that diagnosis. I do not believe, however, that the diarrhea was caused by a bacterial infection.

We have, of course, to consider pancreatic disease as a source for diarrhea, and there I think we are

getting a little warmer in this case, because we know that there was a disordered pancreas in the family background. If she had a disordered pancreas, what was the type? The laboratory data are of no help to us, because if she had sprue we should have a better description of the stools, which I should expect to be described as foul, grayish and fatty containing; but nothing is said except that the stools were thin and watery and finally contained blood.

DR. BENJAMIN CASTLEMAN: They were not fatty.

DR. CHAPMAN: Another disorder of the pancreas that can lead to this picture and give stools of that character is Chiari's disease.¹ He described four conditions in the pancreas that can cause a disturbance of this sort: cystic degeneration; fibrosis; a condition that is rather unusual, phlebitis of thrombosis in the venules in the pancreas; and hemorrhage and necrosis.

I was interested to note that she had clubbing of the fingers. Why should her fingers be clubbed? X-ray films of the chest did not point to pulmonary disease, although it says there was "slight increase of the lung markings." Andersen and his associates² have described cystic degeneration of the pancreas associated with bronchiectasis in the lung, and diarrhea was a prominent feature of the disease. Might she have had this syndrome? There is nothing in the evidence to support it, but one certainly has to mention it.

The last condition to consider is disease of the liver. There are facts in the story that point to primary liver disease in this patient. We know that two and a half years before entry she had anorexia, nausea, vomiting and discomfort in the right upper quadrant, which is anatomically the region of the liver. Following this she had what was said to be "catarrhal jaundice" and thereafter went downhill. In addition, sugar appeared in the urine. Liver disease commonly causes a disturbance in glucose metabolism and has been confused with diabetes mellitus. In further support of liver disease is the low total protein and the high prothrombin time. It is too bad that a cephalin flocculation test or some other test of liver dysfunction was not done. This matter of jaundice appearing and going away is quite surprising, but she must have continued to have jaundice because later the van den Bergh test was 3.3 mg. direct and 8.4 mg. indirect.

If this patient did have some kind of liver trouble, what was the type? It certainly was not portal cirrhosis. Did she have biliary cirrhosis? I cannot say. There is no evidence to support that diagnosis. She did not have a palpable spleen or a big liver, but she did have ascites, and when she was given fluids, she even developed edema. The description of death in the last paragraph sounds to me like that of a patient dying in cholemia.

here is one other rare disease that should be mentioned, another Chiari's³ disease, not in the creas but in the liver, — I have been fooled by once before here,⁴ — that is, a thrombophlebitis of the liver venules themselves. It is a most bizarre nature and is usually seen in older people with carcinoma. This was a young girl, so that we do not suspect carcinoma.

In conclusion, I am forced to make one choice. I have mentioned five possibilities in their increasing order of likelihood. I am going to end up with the final choice that this patient had some type of liver disease, probably Chiari's syndrome. Possibly she had a combination of two of his syndromes, not only a thrombophlebitis of the pancreas but also a peculiar type of cirrhosis following thrombophlebitis of the liver venules. It would not surprise me if she also had bronchiectasis.

DR. FRANCIS D. MOORE: The patient entered on the medical service and was seen in consultation by the surgical service. Most of us lacked Dr. Chapman's diagnostic acumen and were not convinced that there was any pre-existing pathologic process. Her general appearance was thoroughly compatible with one of the extremely sick patients with ulcerative colitis. Clubbing of the fingers has been a repeated observation in ulcerative colitis. This girl had less ascites than some patients with ulcerative colitis. When present, it must be due to the fact that the whole colon is involved as a single tubular abscess and the permeability of the capillaries is increased, so that they pour fluid out into the abdomen as well as into the bowel. She had an ileostomy, and it is routine to resect 1 or 2 cm. of ileum, between clamps, and send it to the Pathology Department to determine whether the disease has extended into the ileum, which is a gloomy prognostic sign. This girl did have ulceration there. The story from there on is up to Dr. Castleman.

CLINICAL DIAGNOSES

Chronic ulcerative colitis and ileitis.
Cardiovascular collapse
Operation: ileostomy.

DR. CHAPMAN'S DIAGNOSES

Ulcerative colitis and ileitis.
Liver disease (? Chiari's syndrome).
Cholemia.
Bronchiectasis?

ANATOMICAL DIAGNOSES

Ulcerative colitis, involving entire colon and distal ileum.
Acute hemorrhagic hepatitis, superimposed on toxic cirrhosis.
Fatty vacuolization of liver, severe.
Operation: terminal ileostomy.
Splenomegaly.

Hemorrhage from mucosal and serosal membranes.
Ascites.
Pulmonary edema and congestion.
Anasarca.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this girl showed an extremely acute, as well as a chronic, ulcerative colitis involving the entire colon and the lower 75 cm. of the ileum. There were numerous ulcers, both longitudinal and transverse, without any bridging such as one sees in the more chronic stages, but there was a lot of edema in both the mucosa and the wall. Microscopic sections confirmed a non-specific acute ulcerative process. We looked hard for amebas but could not find any. The appearance was not inconsistent with what we see in other cases of ulcerative colitis, but as Dr. Chapman implied, that was not the whole story, and he rightly cited the liver as one of the sources of her trouble. The liver presented a striking appearance. Although it was normal in size, weighing 1500 gm., it was composed of bright-yellow fatty irregular nodules, each apparently surrounded by a deep red cuff (Fig. 1). At first we thought that this was a characteristic acute and subacute yellow atrophy of the liver and that these yellow areas were areas of regeneration, the rest being areas of frank necrosis. It would be a little unusual, however, for a person with that amount of necrosis — although there was a lot of regeneration — not to have had more jaundice. Most patients with subacute yellow atrophy are severely jaundiced. Microscopically these nodules were areas of regeneration with extreme fatty vacuolization. The nodules were surrounded by fairly dense connective tissue in which there was extensive hemorrhage.

We know that in ulcerative colitis the almost constant finding at autopsy is a marked fatty vacuolization of the liver, and we can explain all these fatty changes within the regenerated liver nodules as having been due to ulcerative colitis. So this is an example of a healed atrophy type of cirrhosis, the acute attack probably having occurred two and a half years before entry, when she was sick for two and a half to three months. At that time a fair amount of liver tissue was destroyed, this being followed by regeneration. She had recently developed an acute hemorrhagic process of the liver that had little effect on the regenerated nodules. It is quite possible, as has been shown by MacNider⁵ experimentally, that regenerated liver cells are more resistant to another toxic attack than are normal liver cells. Perhaps the ulcerative colitis was just a manifestation of the liver disease. We have never seen it so severe as this, but some of the cases of epidemic jaundice that are now being seen in the Army have shown marked edema and inflammation of the colon.⁶ I should think that it is fair to assume

that the fundamental disease nine years before entry was ulcerative colitis, that two and a half years before entry the patient developed liver disease and that perhaps the toxins derived from the ulcerative colitis produced this further liver damage.

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FIGURE 1. Photograph of Liver

DR. FULLER ALBRIGHT. The veins were all right?

DR. CASTLEMAN: It was not Chiari's syndrome.

DR. MOORE: It is interesting that during the same week that this patient died Dr Altschule and his associates,⁷ of the Beth Israel Hospital, reported the cases of 16 or 18 patients who had had catarrhal jaundice at various periods of time up to many years previously. They had subclinical jaundice, as evidenced by an elevated van den Bergh, and it is interesting that of this small group, two had chronic diarrhea and one had frank ulcerative colitis.

DR. CASTLEMAN: I suppose it is possible that the cirrhosis went back more than two and a half years and that the first attack of diarrhea nine years before entry resulted from hepatic disease. I do not know any way of telling, however.

DR. WILLIAM B. BECKMAN: We had a patient with primary liver disease who during the last six or eight weeks of life developed severe ulcerative colitis. We never knew what kind of liver disease it was.

DR. CASTLEMAN: It is striking that Lucké,⁶ who worked up the cases of epidemic jaundice for the Army, had a number with involvement of the colon.

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CASE 30492

PRESENTATION OF CASE

A fifty-one-year-old housewife was admitted to the hospital because of a productive cough.

Six months prior to admission the patient noted a tickling sensation in her throat that caused her to cough and raise sputum. This increased until she was raising about half a cupful of thick green sputum daily, most of it in the morning. During this period she had lost 10 pounds in weight, and noted diminished vigor. Some tenderness was present over the right lower chest. There was no hemoptysis, night sweats, fever or dyspnea.

Two months before entry a roentgenogram of the chest was taken by a physician who recom-

ended a bronchoscopy. This was performed two weeks before admission, and she was told that she had "congestion" in her lungs. She was referred to the hospital for further study.

The patient had had a cholecystectomy twenty years previously. Two months before entrance into the hospital a tumor of the right breast, apparently without sign, had been removed.

Physical examination on admission revealed a well-developed, well-nourished woman, not acutely ill.

The lower anterior portion of the right chest

size, but the interlobar septum between the upper and middle lobes was slightly low. A Bucky film revealed the trachea to be normal, and its bifurcation and both main bronchi were well outlined. The lower lobe bronchus could not be followed beyond the mass. An intravenous pyelogram showed prompt dye excretion and normal calyces, pelves and ureters. There was evidence of considerable pressure on the bladder, particularly on the right, but no definite soft-tissue mass was visible and the organ emptied normally.

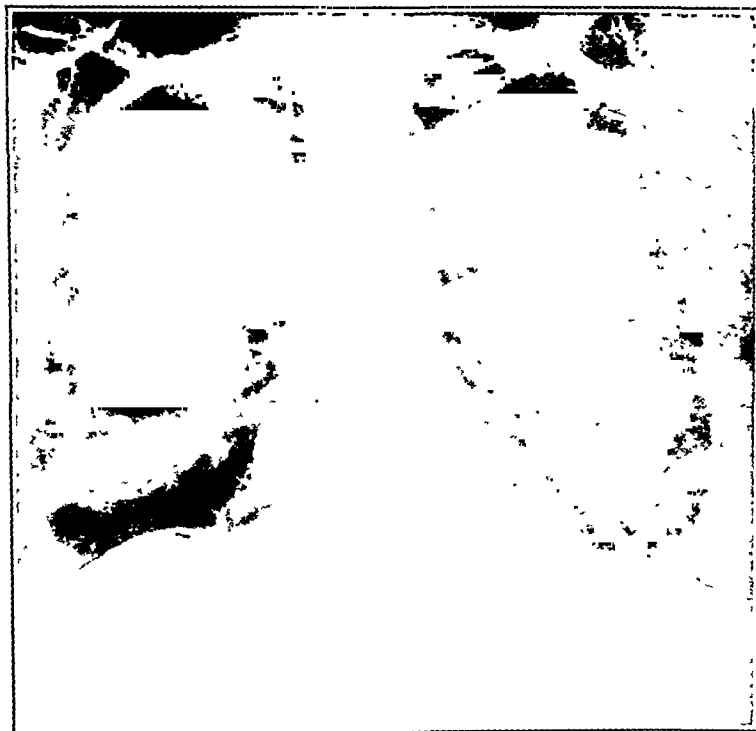


FIGURE 1. Roentgenogram of Chest.

was tender and dull to percussion, with many moist and crackling rales. A small umbilical hernia was present, and there were marked varicosities of the veins of the lower extremities.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 80 diastolic.

Examination of the urine was essentially negative. A blood Hinton test was negative.

A roentgenogram of the chest revealed an ovoid area of increased density measuring 7 by 4.3 cm., lying across the right lower lung field in the region of the lower lobe (Fig. 1). It was outlined fairly sharply and contained a fluid level. Areas of calcification were present along the lower margin of the mass. The heart and mediastinum were displaced slightly to the right. The remainder of the lung fields was clear. In the lateral view the right lower lobe did not appear to be much reduced in

A bronchoscopy on the second hospital day revealed considerable grayish-white, rather sticky secretion throughout the right bronchial tree. The bronchus of the right lower lobe was reddened and a little edematous, but there was no narrowing. The findings were thought to be consistent with chronic bronchitis.

On the ninth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. LAURENCE L. ROBBINS: I shall not attempt to discuss this case from the clinical standpoint. The roentgenologist is usually asked to examine the patient, make up his mind concerning what the fundamental process is and then use the clinical evidence to arrive at a diagnosis. Consequently let us go at this purely from the roentgenologic approach. Let us look at the intravenous pyelogram

and try to eliminate the urinary tract, because I am going to spend most of the time on the chest findings. So far as I can see, the kidney shadows are normal. There is perhaps a questionable mass in the pelvis, but nothing definite except evidence of pressure on the superior surface of the bladder. So far as the bones are concerned they appear normal for the patient's age, except for some degenerative changes around the lumbosacral joint, and in some films there is a questionable defect in the lateral masses of the fifth lumbar vertebra, which suggests that the patient may have had a spondylolisthesis. I shall discard what goes on in the abdomen. It is going to be embarrassing if the operation on this patient turns out to be abdominal, but I can see nothing from the x-ray standpoint that indicates interference in that part of the body.

The films of the chest show an ovoid lesion. To approach it from an anatomic standpoint, where is this lesion? It appears to be fairly well surrounded by air but extends rather close to the pleura posteriorly. It lies in the right lower lobe, probably in the posterolateral division of this lobe. What are the other features of this mass? It is fairly smooth in outline, contains fluid and air, and in the lower margin of the mass there appear to be flecks of calcification. The wall of the mass is thin, although we do not know whether that is true regarding the entire circumference. Fluoroscopy would be helpful because one could tilt the patient from one side to the other to change the level of fluid and thereby get a better view of the wall.

What else is going on within this lobe? Perhaps it is a little smaller than usual, and I think that the septum between the middle and the lower lobes lies farther posterior than is the usual finding. Also, some of the bronchi are perhaps slightly dilated.

In regard to differential diagnosis, the first question is, Is this a tumor? Yes, it could be a primary tumor that had become necrotic in the center and was draining through a bronchus. One factor against that is the rather thin wall, and where we are able to visualize it, the lesion appears to be fairly smooth in outline. Could it be metastatic tumor from carcinoma or sarcoma elsewhere? Yes, but it is rather rare for metastatic lesions to break down and drain into a bronchus. Could it be a lymphoma? Lymphoma of the lung is relatively rare, and in the few cases that I have seen, it has not broken down; nor have I seen calcification within it. That more or less covers the group of tumors. I cannot completely rule out carcinoma, but it does not seem likely.

Could it be a tuberculoma? It is in the lower lobe, and in the few cases that we have seen the majority of the lesions have been in the upper lobe. The calcification would go with tuberculoma. We shall have to wait and see if we can find anything in the clinical findings that will be of help.

Could it be an abscess? If it were an abscess, I should think that it would be on the basis of inhalation or associated with bronchiectasis. The calcification in the wall could go with long-standing abscess, and the rather thin wall could again go with it, because it would mean that the abscess had been present for a long time, developed a capsule and was well localized. I do not believe that it was an abscess on the basis of a septic infarct because that usually clears in a relatively short time, and in the cases that we have seen they have not localized quite so well as this.

Then we come to the possibility of bronchiogenic cyst, or what is often called a "hamartoma." So far as I can gather, the difference between a true bronchiogenic cyst and a hamartoma is essentially that the cyst contains more glandular material within it and secretes the mucoid material that is so characteristically found in these cysts. It certainly could be a bronchiogenic cyst that had become necrotic and was draining through a bronchus. I do not believe that the calcification within the wall is against such a diagnosis.

I have covered the x-ray examinations fairly thoroughly, and in general my interpretation has not varied greatly from the original one. Now let us turn to the clinical findings to see if we can get any further information. We have the story of a patient raising large amounts of sputum, which is consistent with bronchiectasis or an abscess or a bronchiogenic cyst that had become infected and drained into a bronchus. I still cannot rule out necrotic tumor, but there is no evidence of hemoptysis, which is of considerable importance. A previous x-ray examination for comparison would be a tremendous help. We do not have that by any chance?

DR. BENJAMIN CASTLEMAN: No.

DR. ROBBINS: In the past history we find that the gall bladder and a tumor of the right breast had been removed, which raises the remote possibility of metastatic tumor. But for the reasons that I have given we shall disregard that diagnosis. It is difficult to explain the physical findings entirely by the lesion in the chest. There is, however, a shadow in the anterior costophrenic angle that may or may not be of significance. The number of things that it could be in that area are legion, and I am not going to get mixed up in a discussion of them. So we come down to the fact that this patient had had a six-month story of raising fairly large amounts of sputum in the morning. I cannot take a definite stand and say whether this was due to a lung abscess, tuberculoma or infected bronchiogenic cyst, but I am inclined to put the most emphasis on a long-standing lung abscess, even though the history does not exactly fit in with it, and put as my second choice an infected bronchiogenic cyst.

DR. CASTLEMAN: Are there any further questions?

DR. HELEN S. PITTMAN: I should put abscess first on the list. I think that it is surprising, however, that it was an abscess, that the patient had no fever and no elevated white-cell count. There is no mention of the sputum. If it were an abscess, I would expect the sputum to be unpleasant enough so that there would have been a note about it somewhere.

DR. RALPH ADAMS: I believe that it was a bronchiogenic cyst, not a chronic lung abscess and not a malignant tumor with central necrosis. It seems to me that a lung abscess of six months' duration would have had a wall that was thicker than the apparently thin wall in this case. Furthermore, the sputum in a lung abscess with the amount of sputum that she would, almost certainly, have been foul and very likely would have been bloody. The tumors with central necrosis have, by and large, the so-called "sore thumb" sign. One sees air at the top of the cyst and a suggestion of fluid level, but here it is piling up in the center, which has come to be recognized as the tumor seen in profile. In addition, a malignant tumor, particularly if it is breaking down, almost always causes hemoptysis. For these reasons I think that the lesion was a bronchiogenic cyst.

CLINICAL DIAGNOSIS

Bronchiogenic cyst.

DR. ROBBINS'S DIAGNOSIS

Lung abscess?

Bronchiogenic cyst, infected?

ANATOMICAL DIAGNOSES

Lung abscesses.

Bronchiectasis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The patient was operated on and the right lower lobe was removed. There were no adhesions over the surface of the lung, and apparently the surgical procedure was not particularly difficult. We were able to feel a hard mass within the lobe, and the surgeon, before removing the lobe and therefore before the surrounding lung had collapsed, reported that the mass was extremely hard; because of this and because he was unable to feel any fluctuation, he toyed with the idea that it was a tumor.

After fixation the lung was sectioned. In the central portion of the lobe we were able to find three cavities, two communicating with each other, but separate from the others. They all communicated with a major bronchus (Fig. 2). The walls were thin, measuring only 1 mm. in thickness

in most places. The inner surfaces of these cavities were granular, and microscopic studies showed no evidence of tuberculosis. All the cavities were lined by bronchial mucosa, and I therefore believe that they were abscesses, perhaps bronchiectatic, rather than bronchiogenic cysts. I do not suppose there is any real way of proving this except that the walls were exactly like that of a bronchus. One did not have to hunt for the various bronchial elements in

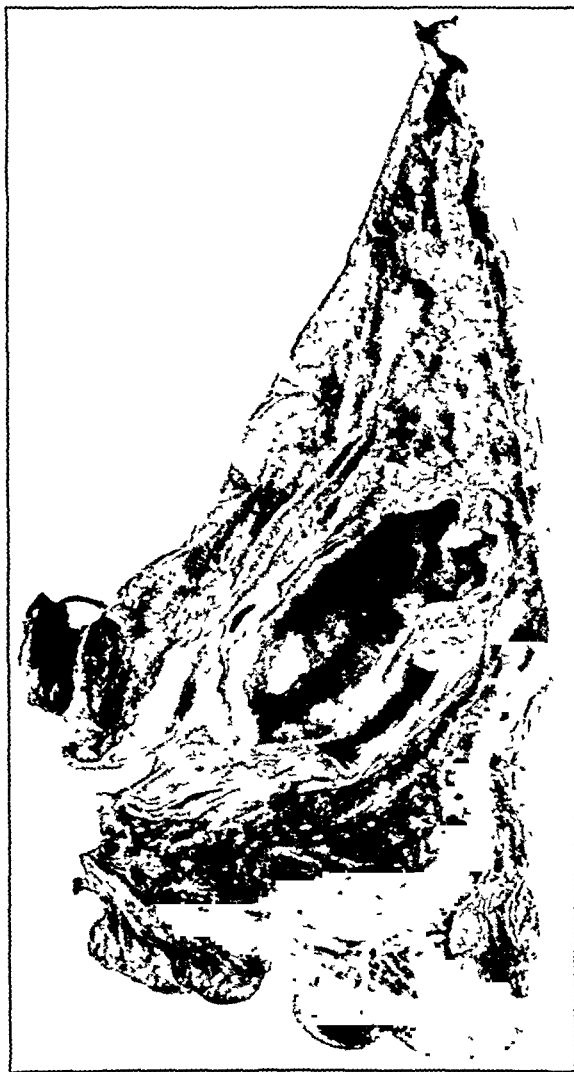


FIGURE 2 Photograph of Resected Right Lower Lobe.

the wall as one usually does in bronchiogenic cyst. Whether this was a bronchiectasis with abscess formation or whether it started out as an abscess and secondary bronchiectasis developed I do not believe that anyone can say. The fact that there was no involvement of other bronchi is suggestive that it started as an abscess, which later communicated with a bronchus. That there were three of them is also in favor of their being abscesses.

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THE CHRISTMAS SEAL CAMPAIGN

THE seriousness of the tuberculosis problem is strikingly shown by statistics recently issued by the National Tuberculosis Association. One out of every hundred men examined for military service has been disqualified by having the disease — 30 per cent showing it in a clinically active form. Furthermore, in the thirty-one months after Pearl Harbor the deaths from tuberculosis in the United States were nearly three times those occurring in combat — 145,000 against 57,000.

Although the tuberculosis death rate has been reduced 75 per cent in the last forty years, its ravages continue, in spite of the fact that the means of prevention and cure are well established. Fifty-six thousand people in this country died of tuber-

culosis last year, and it is estimated that over a million people have the disease, only half of them being known cases. In the war-torn countries of Europe the problem is, of course, ever so much more serious. In the United States, indications point to a reversal of the downward trend of mortality unless drastic steps are taken to prevent it.

These facts give special importance to the approaching Christmas Seal Campaign. The fund thus raised will be devoted to widely publicizing x-ray examinations of the chest, to the follow-up and treatment of cases thus discovered and to many kindred activities in the fight against tuberculosis. In buying Christmas Seals to the limit of our resources, we shall not only be aiding in a domestic war but in no small measure be contributing toward the military victory that is sure to come.

THE FAT OF THE LAND

SINCE the strict rationing of 40 per cent cream went into effect on August 1, a monthly saving of 2,300,000 pounds of butter fat has been effected in the sixteen federal market areas, according to advices from the War Food Administration. In the face of such startlingly good results from a program that has been none too popular, although ostensibly designed to increase the amount of butter available to the consumer, the rise in the point value of the commodity to the almost prohibitive level of twenty points per pound is unfortunate and is hard to explain to the little people who are supposed to constitute the backbone of the nation. The explanation, however, has been made in a recent broadcast of Mr. John H. Sullivan, district director of distribution of the War Food Administration.

The first reason for the current butter shortage according to Mr. Sullivan, is that the current butter production is 17 per cent lower than the 1935-1939 average. A second reason is that we are sharing our supplies with both American and Allied fighting men. A third is that more people can afford to buy butter than ever before, because wartime incomes are higher; and a fourth, that the increased milk output is not going into butter but

other uses. Civilians, for instance, are drinking from 20 to 25 per cent more milk than formerly, and the armed forces have asked the manufacturers for evaporated and condensed milk for a 75 per cent increase in these products over last year.

Despite a 14 per cent increase in milk production since the years before the war, butter production, it has been indicated, has fallen off 17 per cent. Of the butter manufactured, 80 per cent of the total is available to civilians. 15 per cent is set aside for military purposes, and 5 per cent goes to Russia for use in military hospitals. The average civilian share will be something less than twelve pounds per person this year, as compared with nearly seventeen pounds between the years 1935 and 1939.

It is a poor American, indeed, who will not make enlightened sacrifices to help in winning the war, although he may still wonder why all but two and a half of his weekly red points are required to secure this allotted butter ration. Those of us who have seasoned our patriotism with philosophy, however, will continue cheerfully to do without heavy cream, and will learn that oleomargarine is an excellent substitute for the theoretical twelve pounds of butter.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON POSTWAR PLANNING

The first meeting of the Committee on Postwar Planning, appointed by the President of the Massachusetts Medical Society, was held on November 8 with twenty-three members present. Important topics considered for committee action included the problem of providing both short-term and long-term residencies and refresher courses to medical men returning from service, the place of the hospital in postwar education, opportunities for doctors in public health and the relation of medicine to changing economic conditions.

The Committee begs the interest and co-operation of the members of the Society and asks that questions be sent to the chairman. Information bureaus at the headquarters of the American Medical Association and, for Massachusetts, at 8 Fenway, Boston, are expected to help physicians returning from service.

HOWARD F. ROOT, *Chairman*

DEATHS

BAUMAN — Julia L. Bauman, M.D., of Holyoke, died November 17. She was in her sixty-third year.

Dr. Bauman received her degree from the Women's Medical College of Pennsylvania. She was reputed to be the first woman of Polish birth to practice medicine in Massachusetts.

DRAPER — Frank E. Draper, M.D., of Framingham, died November 24. He was in his eighty-first year.

Dr. Draper received his degree from Harvard Medical School and studied at Vienna University. He was formerly assistant ophthalmic surgeon at the Massachusetts General Hospital and the Boston Dispensary and clinical assistant at the Massachusetts Eye and Ear Infirmary. He was a member of the New England Ophthalmological Society. He served as a captain in the Army Medical Corps during World War I.

His widow, a daughter, a granddaughter and a great granddaughter survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

USE OF DIPHTHERIA TOXOID IN ADULTS

Diphtheria toxoid is now the universally accepted agent for the immunization of children against diphtheria. It has been extensively used in adolescents and adults as well, but it is prone to cause marked reactions in a certain percentage of these unless small initial doses are used and subsequent doses are adjusted according to the presence or absence of a reaction to the first dose.

Since reactions to diphtheria toxoid in adolescents or adults are most frequent and severest in persons who are immune to diphtheria, it is of course essential that these be excluded from any immunization program by previous Schick testing. By taking this elementary precaution and by starting with a small initial dose (0.1 cc.) as indicated above, it is entirely practical to immunize adolescents or adults with diphtheria toxoid.

The practice of immunizing such persons with diphtheria toxin-antitoxin mixture has been abandoned almost everywhere, since toxin-antitoxin is less efficient than toxoid as an immunizing agent, and also because it necessarily contains serum from a horse or other animal. For these reasons, the use of toxin-antitoxin for individual immunization is no longer recommended, and the department will discontinue the distribution of the package containing three 1-cc. vials of toxin-antitoxin as of January 1, 1945.

Since the routine use of diphtheria toxoid in groups in which individual adjustment of the dosage is not practical is not as yet entirely satisfactory, toxin-antitoxin mixture in 20-cc. vials will continue to be furnished.

Interpretation of the Schick test. The usual instructions for interpreting this test state that subjects showing positive reactions with toxin and positive but smaller reactions with the control material are susceptible to diphtheria but are also sen-

sitive to the proteins of the diphtheria bacillus. Such persons are *exceedingly* likely to react either to toxin-antitoxin mixture or to toxoid, and should be immunized cautiously, if at all. Recent experience suggests that many such subjects are actually immune to diphtheria. Whenever there is doubt concerning the best immunizing procedure to follow, it is suggested that the person in charge consult the director of either the Division of Biologic Laboratories or the Division of Communicable Diseases regarding the advisability of determining the patient's serum antitoxin titer. This test which can be done in four or five days, is a valuable method for determining the patient's immunity. It can be carried out with 5 to 10 cc. of blood sent, preferably in a sterile tube, to the Antitoxin and Vaccine Laboratory.

BOOK REVIEW

Medical Clinics on Bone Diseases: A text and atlas. By I. Snapper, M.D. 4th, cloth, 225 pp., with 30 plates and 39 tables. New York: Interscience Publishers, Incorporated, 1943. \$10.75.

This monograph will prove stimulating to internists, surgeons, endocrinologists, roentgenologists and orthopedists. The author has had a wide experience in Amsterdam and later as professor of medicine at the Peiping Union Medical College in China, and he draws liberally from it in this critical review of recent concepts of certain of the bone disorders. The text is built around a group of the author's cases, which are given in considerable detail; the dissertation on each disease condition includes a discussion of the history, pathology, clinical symptomatology, biochemistry, pathologic physiology, differential diagnosis, etiology and treatment. A unique feature is the inclusion of photographic prints of the x-ray films, bound as full-page inserts with the text. As a result, the illustrations are decidedly superior to those usually found in reference books. An extensive bibliography is included at the end of each chapter; an author and a subject index are placed at the end of the monograph.

The author devotes half the monograph to a discussion of conditions associated with hyperfunction of the parathyroid glands, both primary and secondary. He discusses, among other topics, von Recklinghausen's observations, classic osteitis fibrosa cystica with gross bone involvement, renal complications of hyperparathyroidism, with and without involvement of the skeleton, gastrointestinal symptoms from hypercalcemia, differential diagnosis of hyperparathyroidism, and various phases of parathyroidectomy. Although the general discussion is excellent, the interpretation given to some of the investigations quoted from the literature are misleading and tend to undermine confidence in the rest of the work. Little discussion is made of the point that bone disease need not develop in patients with hyperparathyroidism if sufficient calcium and phosphorus are ingested in the diet; as a corollary to this, the author is reluctant to admit the existence of cases in which the only demonstrable pathology is in the renal system, although these are commonly found by physicians on the alert for them.

Hyperparathyroidism secondary to osteomalacia and chronic renal insufficiency are discussed. To the reviewer, this chapter seems rather confused. Although in an earlier section the author calls attention to the fact that acidosis induces osteitis fibrosa, he gives little consideration to acidosis as a cause of the bone lesions in the cases with chronic renal insufficiency; furthermore, he does not discuss the effect of correcting the acidosis on the bone lesions or on the abnormal calcium and phosphorus levels in the blood. He notes that some cases have hyperphosphatemia because of phosphate retention and that some cases have hypophosphatemia,

which he believes is due to osteomalacia from poor diet and lack of sunlight instead of hyperparathyroidism; does not discuss the hypocalcemia in these cases as a cause of excretion in the urine of calcium as a fixed base to the acidosis.

The author gives an interesting account of osteitis fibrosa as it is found in China, where poor diet and lack of exposure to sunlight combine to produce avitaminosis D. In the United States, however, osteomalacia is commonly seen only as a result of steatorrhea from such disorders as nontropical sprue or pancreatic disease; no discussion of these conditions is included. This section would also have profited from some consideration of the effect of vitamin D on calcium and phosphorus metabolism. Excellent chapters are included on Paget's disease of bone, Gaucher's disease and multiple myeloma. The illustrations and the cases in these sections are among the best in the monograph.

A detailed discussion is given of lipid granulomatosis or xanthomatosis of the bones. The author contends at length that osteitis fibrosa disseminata (Albright) or multiple fibrous dysplasia (Lichtenstein) is a manifestation of local granulomatosis of the bones, but his evidence is not convincing. He points out that lipid infiltration is a secondary process even in so-called "lipoid granulomatosis"; hence, secondary infiltration with lipid might reasonably be expected to occur in an occasional case of osteitis fibrosa disseminata. Furthermore, his insistence that lipid infiltration can be demonstrated only in a biopsy of a lesion is difficult to reconcile with lipid infiltration as a secondary process; that is, one would not expect to find it in the earliest lesions.

In the differential diagnosis of hyperparathyroidism, the author considers Paget's disease, multiple myeloma, generalized cancer metastases in the bones, decalcification of the bones in hyperthyroidism, lipid granulomatosis of the bones or xanthomatosis ossium (including osteitis fibrosa disseminata), chronic renal insufficiency and osteomalacia. One is disappointed not to find a discussion of sarcoidosis, lymphoma involving bone, benign metastasizing hemangiomas and osteoporosis. One would like also to have found included in this monograph some discussion of neurofibromatosis, osteopetrosis, the effect of lead and fluoride on bones, hyperparathyroidism and the various conditions causing tetany. The most surprising omission is osteoporosis. This condition, which is considered to result because of a defect in the formation of the matrix rather than in the calcification of it, is not clearly defined in the monograph. At times the author appears to be using osteoporosis as a general term for a rarefied bone. Osteoporosis has been found associated with immobilization and reduction in stress and strain, senility, postmenopausal state, Cushing's syndrome, hyperthyroidism and conditions associated with protein depletion (hunger osteopathy). Osteoporosis has been recognized as one of the commonest metabolic bone disorders, — postmenopausal osteoporosis, in particular, having been widely observed. The author barely mentions a few of these conditions. Exception must also be taken to certain statements. The author speaks of normal calcium and phosphorus metabolism when he means normal levels of calcium and phosphorus in the blood; he states that, in bone metastases from cancer of the prostate, acid phosphatase is constantly present when he means that it is usually elevated above the normal level.

In spite of these criticisms, most of which would be passed over by the casual reader, the monograph is a valuable contribution in a field largely unknown to most physicians. It should find considerable use as a reference work among persons interested in these disorders.

The publishers are to be commended on the mechanical features of the book: it has excellent illustrations, good type, substantial paper, sturdy binding and no typographical errors.

NOTICES

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Harvard Club on Friday, December 15. There will be an x-ray conference at 4:30 p. m. At 8:00 p. m. Dr. Kurt H. Thoma will speak on the subject "Tumors of the Jaw."

(Notices continued on page xv)

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SYMPOSIUM ON GALL-BLADDER DISEASE

A PLEA FOR THOUGHT-TAKING IN THE MEDICAL TREATMENT OF CHOLECYSTITIS*

WALTER C. ALVAREZ, M.D.

ROCHESTER, MINNESOTA

WHEN faced by a patient demanding medicine for a disease for which there is no known or logical treatment, the medical profession has always found it easier to give something than to try to explain why nothing is likely to cure or even to relieve the condition. Unfortunately, most patients will not even stop to listen to such frank speech; they believe firmly in the efficacy of medicine and diet, and they know that there are treatments available for every disease. If an honest physician refuses to give them treatment that he thinks is useless, they usually persist until they find someone who will give them a placebo of some kind.

At first glance this seems to be the best way out for all concerned, but actually it is hurtful to the physician, because after prescribing a placebo for a few years he is almost certain to forget that it never had any basis in scientific fact. He will come to believe in its efficacy, and if he is a writer, he is likely soon to be listing and even praising the medicine in his articles and textbooks. Then, if someone comes along who questions the logic of its use or its efficacy in practice, he is likely either to ignore the doubter or to become angry with him for his silly caviling.

Throughout the United States today the current medical treatment for cholecystitis is a diet low in fats and a prescription for some proprietary pill containing usually bile salts or bile salts with some cheap laxative, such as phenolphthalein. The two questions that should arise in one's mind are, How logical and scientific are these prescriptions, and do they do any good? In the first place, why should a person with a diseased gall bladder avoid fats? Originally the idea probably was that bile helps in the digestion of fats, and that hence when there is disease in the biliary tract fats should be avoided. Actually, in all cases of cholecystitis without jaun-

dice, the bile is flowing from the liver into the duodenum without hindrance, and in many cases the cholecystogram shows that the gall bladder is still doing fairly well in concentrating the bile. In other cases, the only defect is that in the intervals between meals the bile is not being stored properly in the gall bladder. In this event, it cannot be poured out in the usual concentration to meet the food when it enters the duodenum.

But if patients with cholecystitis frequently suffered from an imperfect digestion of fats, one would expect them often to have diarrhea with fatty stools and a progressive loss of weight, but this is not the case. Most of the patients suffer from constipation, and many digest so well that they gain in weight. My impression, gained from talking to scores of persons who have been on a low-fat diet, is that it did not make much difference in their digestive comfort. Many had a good digestion to begin with, and many of those who suffered with flatulence and a feeling of heaviness in the abdomen said that the secret of avoiding trouble was never to eat a *big meal* or a meal consisting of rich foods of any kind. A few had learned that certain foods like onions, cabbage or raw apples tended to cause trouble, and they had obtained some relief by leaving these foods alone.

Curiously, no one seems to have thought that the patient who has had a nonfunctioning gall bladder removed surgically is no different physiologically from what he was before the operation, and yet after the operation he is generally told to eat what he pleases, and he digests usually everything he eats. No one thinks of putting him on a diet. From this it must be concluded that the indigestion of cholecystitis is usually not due to any lack of concentrated bile in the upper part of the small intestine, and that hence there is no need of always barring fat from the diet.

Another reason sometimes given for the avoidance of fats in the diet of patients with cholecystitis is

*This paper and the two that follow were presented at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944. From the Division of Medicine, Mayo Clinic.

that with a low intake of cholesterol the formation of gallstones may be avoided. There is no evidence in the literature that this precaution is worth taking, but granting that it is in some cases, it cannot be worth taking in the many cases in which the gall bladder is so packed with stones that it would be impossible to get any more in.

A diet sufficiently low in fats and carbohydrates can, of course, help by reducing the weight of the patient if he or she happens to be stout, but there is no reason for expecting this to restore a badly diseased gall bladder to a healthy state. According to some German writers, the restricted diet forced on Europeans by World War I cut down the frequency of colic in patients suffering from gallstones.

Interestingly, it has repeatedly been shown that if one wants to "flush out" the gall bladder by emptying it as thoroughly as possible, the best way to go about it is to give fats such as cream and egg yolk. According to Boyden, Sosman, Whitaker, and others,¹ fats cause the gall bladder to contract more forcibly and to empty more completely than does the magnesium sulfate that has so often been used for this purpose. To be logical, then, it seems that physicians should often be prescribing a diet rich in fats for patients with cholecystitis. To avoid fats in the diet is to invite stagnation of bile in the gall bladder. This favors excessive concentration of the bile, which in turn favors the formation of stones. The sensible thing to do is to have a patient restrict his intake of fat when a trial shows that this makes him more comfortable.

The pill containing bile acids is probably given with the idea that these substances will cause the bile to flow faster, that with this there will be a flushing out of the gall bladder, and that with the flushing there will be a clearing away of infection, and perhaps some washing out of small stones. According to Phibbs, Wigodsky and Ivy,² several investigators, among them Taterka, Impallomani and Jankelson and Altman,³ found that the giving of bile salts results in an increase in the size of the gall bladder, which indicates that with the more rapid flow of bile out of the liver there is an increase in the flow into the gall bladder. That there is no great increase in the flow out of the gall bladder and therefore no flushing effect with bile acids was shown by Phibbs and his associates when they gave ketochol, a mixture of bile acids, to dogs. There was no sign of any change from normal in the concentration of bile in the gall bladder.

But even if one could produce a greater flow of bile in and out of the gall bladder by increasing the rate of flow down the common duct, it is hard to see how this could help many patients with cholecystitis, because in this disease the infection, when demonstrable, is found not so often in the bile as deep in the muscular wall of the gall bladder. Moreover, any flushing that may be effected can hardly have any influence on stones that are too large to pass through the cystic duct. The flushing of smaller

stones into the common duct, if it could be accomplished, would probably do the patient harm rather than good. Certainly, there is no possibility of any flushing in the many cases in which the gall bladder is too badly diseased to have any function, or in which it is packed with stones or sand, or sealed off from the ducts by a stone imbedded in its neck.

Some may ask, "How about the Meltzer-Lyon type of treatment for cholecystitis?" My answer is that I never could see much logic in it and hence I have never used it. So far as I can tell, it has gone out of fashion and is seldom used today.

It would perhaps be best for the mental development of all physicians if they would oftener admit that there is no logical medical or dietary treatment for cholecystitis, especially when bile has ceased to flow easily into and out of the gall bladder, or when the organ is full of stones or its wall is stiffened with scar tissue and full of bacteria.

To those physicians who say, "But our treatment works perfectly in a high percentage of cases," the answer is that the physician who does nothing for his patients with chronic cholecystitis can point to scores of cases in which for years the man or woman has not had a pain or an ache; he, too, is getting beautiful cures. Cholecystitis being the disease that it is, with its tendency to remissions of symptoms lasting twenty years or more, no one can tell when a treatment was responsible for an apparent cure and when it was not. When, as often happens, I see old persons who have "gotten by" comfortably enough, carrying gallstones for ten or twenty or thirty years, I wonder if I should not avoid surgical treatment as often as I can, but when, as also often happens, I see someone who loses his life because a diseased gall bladder was not removed in time, I wonder if I should ever permit a person with definite cholecystitis to go without operation.

Usually, the person whose gall bladder is beginning to cause a good deal of pain and flatulence had better have it out. I recommend immediate operation also to those persons with a bad gall bladder who have to travel much or live in out-of-the-way places where a good surgeon is not available. I am not inclined to recommend operation when there are one or two stones in a functioning gall bladder and the symptoms, if any, are not those of cholecystitis.

* * *

All this is really a plea for thoughtfulness and specialization in the treatment of cholecystitis, and a protest against the unthinking treatment of all cases with the same diet and the same mixture of bile acids and a laxative.

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3. Cited by Phibbs, Wigodsky and Ivy.²

THE SURGICAL ASPECTS OF GALLSTONES

HOWARD M. CLUTE, M.D.,* AND FRANCIS R. KENNEY, M.D.

BOSTON

AMONG lay people and many physicians as well, there is a deeply grounded belief that gallstone surgery is dangerous and is not to be advised until repeated attacks of indigestion, pain and jaundice make it absolutely inevitable. It is our belief, however, that gallstones can be safely removed if the operation is undertaken before complications have occurred. Furthermore, in the great majority of cases of simple or silent gallstones an early elective cholecystectomy is wiser than an operation into which one is forced by the complications of the disease. There is far too great a tendency to worry unduly about gallstone surgery and to forget the dangers that gallstones may produce.

Gallstone surgery is, however, decidedly major surgery, and requires far greater skill than do most surgical procedures in the abdomen. There is no question that the occasional operator can do as much or more harm in operating on the biliary tract than will result from many of the disease conditions he is treating. Strictures of the common duct, duodenal injuries and fistulas, overlooked cystic and common-duct stones — these are some of the penalties exacted by ill-advised attempts at surgery of the biliary tract. It is most important that the surgeon who elects to operate on biliary-tract disease shall be well trained and thoroughly experienced in the technic of the procedure. The dangers of gallstones lie first in the complications that they may produce and secondly in the surgery required for their removal. These dangers can to a large degree be avoided by the performance of operation before complications occur and by a better quality of surgery.

From January 1, 1935, to December 31, 1943, we operated on 356 patients with chronic cholecystitis, with or without gallstones, and its complications. This series does not include 179 patients with other types of biliary-tract disease not immediately related to gallstones who were seen during this period. In Table 1 are listed the types of biliary-tract disease encountered and the operative mortality of each.

The removal of the gall bladder for chronic cholecystitis with stones or with cholesterosis is now a completely safe procedure. In 201 cases in which operation was performed — 178 with and 23 without gallstones — there was only 1 death, a mortality rate for simple cholecystectomy of 0.5 per cent. The cause of this death was never clearly understood, since autopsy was not per-

mitted. The patient was a woman of thirty-five in good condition. The gall bladder was removed for cholesterosis and the common duct was explored; it contained no stones. Death, apparently

TABLE 1. *Types of Biliary-Tract Disease.*

TYPE OF DISEASE	No. OF CASES	DEATHS	
		NO.	PERCENTAGE
Chronic cholecystitis:	201	1	0.5
With gallstones	178	0	
Without gallstone	23	1	
Acute cholecystitis	71	5	7.0
Stones in the common duct	84	8	9.5
Totals	356	14	
General average			3.9

from shock, occurred fifteen hours after the operation. There was no evidence of hemorrhage. Thus, the only fatality in 201 patients receiving cholecystectomy for uncomplicated disease of the gall bladder was probably due to an unknown error in surgical technic or to a failure to prepare the patient more carefully for operation. The important point is that simple gallstones can be treated safely. The danger of surgery in these cases has been reduced to a minimum by the co-operative efforts of the internist, the anesthetist and the surgical team in their preoperative, operative and postoperative care.

No longer is a patient with simple gallstones seen one day and operated on the next. Time is taken to be certain that the symptoms are due to the gallstones and not to some other trouble, such as heart disease. Tests of kidney function and liver function are carried out. If anemia is present, iron therapy and transfusions are given. Extra fluids, glucose and proteins are administered to improve liver function before surgery is undertaken.

The anesthesia in surgery of the biliary tract plays a particularly important role. A gentle, short, easy operation under the complete relaxation of spinal anesthesia appears to be far safer than a long, difficult one under the incomplete relaxation of many other anesthetic agents. We realize that we are particularly fortunate in having an outstanding anesthetist associated with us, to see all cases before operation and to decide with us regarding the operative risk and the best type of anesthesia. If we could not have a trained anesthetist to give spinal anesthesia for gallbladder surgery we should use ether — or postpone the surgery. Spinal anesthesia should not be used in upper abdominal surgery unless it can be given and supervised by an experienced and well-trained anesthetist.

The postoperative use of parenteral fluids, blood transfusions and oxygen and frequent turning of the patient are of great value in keeping the surgical

*Professor of surgery, Boston University School of Medicine, surgeon-in-chief, Massachusetts Memorial Hospitals; surgeon, New England Baptist Hospital.

mortality of gallstone operations low. Each case should be followed by the surgeon himself to make certain that these measures are properly carried out. In this type of surgery routine orders cannot replace individual attention.

We and other surgeons have in the past stated that exploration of the common duct in gallstone surgery does not increase the risk and that it prolongs the hospital stay by only a few days, if at all. This viewpoint we have come to question. There is, of course, no doubt in anyone's mind that the common duct must be opened if there are positive indications for it. In a great many cases, however, there are definite indications that no stones are present in the common duct, and that it should therefore be left alone. Anything approaching a routine exploration of the common duct at the time of a simple cholecystectomy for gallstones should be avoided. Reoperation has been necessary in certain cases to remove stones left—or re-formed—in the common duct, but in every one of these the duct had been explored at the first operation. A secondary choledochostomy has not been necessary in any case in which the duct was not explored at the first operation. We now believe that choledochostomy increases the time of the surgery, opens a viscus that is easily damaged, increases the shock of the operation and the chances of postoperative complications and prolongs the hospital stay. Choledochostomy should be done only when positive indications are present. In one third of the 201 cases of simple cholecystectomy the common duct was explored, but no stones were found.

There is no intention to imply that every patient who has simple or uncomplicated gallstones should have them removed. If the patient is not a good operative risk because of old age, hypertension, heart disease or other constitutional defects, no operation for simple gallstones should be undertaken unless it appears that their removal will improve the patient's general health. As evidence of this belief, there were 81 cases not included in this study, with gallstones or probable gallstones, in which surgical removal was not advised. In all such cases consultation is sought before a final decision is reached.

The two most frequent complications of gallstones are attacks of acute cholecystitis and the passage of stones into the common duct. Seventy-one of these patients had acute cholecystitis, with a 7.0 per cent mortality, and 84 stones in the common duct, with a 9.5 per cent mortality. It is difficult to keep the statistics clear, since in some of the cases of acute cholecystitis there were stones in the common duct as well. The important point is that both the complications mentioned carry a serious mortality risk.

It has long been our contention that most cases of acute cholecystitis begin not with a bacterial infection of the biliary tract but with an obstruc-

tion of the cystic duct that interferes with the circulation of the gall bladder. Following this obstruction comes pressure on the veins, the lymphatics and even the arteries, which produces edema, infarction, necrosis and even perforation of the gall bladder. Not until this process is well established—in thirty-six to forty-eight hours—does bacterial invasion occur. Because of this basic course of the disease, immediate surgery within a day or at most two days of the onset of acute cholecystitis and before bacterial invasion occurs is wisest and safest. Delay in these cases means waiting for the onset of infection and for the possibility of perforation of the gall bladder, which occurs in about 20 per cent of the cases.

Operations on patients within twenty-four to forty-eight hours of onset are and should be safe and uncomplicated procedures. Death from acute cholecystitis has occurred in patients who have had repeated attacks of acute cholecystitis that have been "watched." Finally an attack appears that does not subside but goes on to develop infection, abscess formation, cholangitis or perforation and resulting peritonitis. All 5 patients who died from acute cholecystitis had had repeated attacks of the disease, all were between the ages of forty-five and seventy-three, with an average of sixty-one, and all were seen some days after the onset of symptoms—too late for early surgery. The causes of death were coronary infarction in 1 case, peritonitis in 2 cases and septic cholangitis in 2 cases. We are therefore convinced that the factor of delay in operating on patients with acute cholecystitis is responsible for much of the mortality, and that the proper management of these cases is surgery soon after the first attack.

One seldom sees a patient with stones in the common duct who has not had repeated attacks of gallstone colic or acute cholecystitis or both. In fact, when a surgeon operates for gallstones in a patient who has had six or eight or more attacks of colic, he must realize that it will probably be necessary to explore the common duct. Stones in the common duct are a dangerous complication of gallstones, as shown by the fact that 8 of the 84 patients with them died. Each of these patients had had repeated attacks of pain, often over a period of many years. Although 1 patient was only thirty-eight years old, all the others were over fifty-nine and the average age was sixty-three. The causes of death in this group are of some importance. In 3 cases, death followed cardiovascular accidents; in 1, post-mortem examination showed only ileus; in 2, acute generalized peritonitis was found; in 1, gas-bacillus infection had occurred; and in 1, death was apparently due to the so-called "hepatorenal syndrome."

In this group with common-duct stones, other serious disease was often found as a result of the long-standing process. Thus, jaundice was present

at least 20 per cent of the cases, fever and chills were not infrequent as evidence of cholangitis, and a fistula between the duodenum and the gall bladder was present in 3 cases.

All these facts are strong evidence that there is a far too great delay in the surgical removal of gallstones. Such complications occur only in patients who have had gall-bladder trouble for a long time. They represent the end stages of gallstone disease. The degree of permanent kidney and liver damage in the patients who survive surgery cannot be estimated, but it must be a distinct factor in later life.

This study does not include 8 cases of acute pancreatitis, although 6 of these patients had gallstones as well. In some cases there had been repeated attacks of biliary colic that were sufficiently clear to warrant a diagnosis of stones and earlier operation for them. Also excluded are 7 cases with cancer of the gall bladder or bile ducts. What relation, if any, exists between these findings and gallstones is problematic. It is, however, well known that gallstones are present in 65 per cent of patients having cancer of the gall bladder.²

We wish to emphasize the point of this paper by briefly reporting a case recently seen on the Surgical Service of the Massachusetts Memorial Hospitals.

The patient, a 73-year-old woman, had had her first attack of gallstone colic 20 years previously, and attacks had continued at varying intervals subsequently. In 1938, a diagnosis of gallstones was made by x-ray study. In 1940, the patient was operated on in this hospital for obstruction of the small bowel due to a gallstone in the ileum. In the postoperative period she developed phlebitis in each lower leg, auricular fibrillation and cardiac failure. After a stormy convalescence she was discharged. One year later attacks of gall-bladder colic reoccurred. In 1943, she was admitted to the hospital because of recurring attacks of upper abdominal pain, chills and fever. Because of a high blood pressure (230/100) and

arteriosclerotic heart disease, surgery was not undertaken. Early in 1944, the pains, fever and chills returned and were accompanied by obstructive jaundice. Operation was deemed necessary in spite of the obviously poor risk. A large fistulous opening was found between the gall bladder and the duodenum. Stones were present in both the gall bladder and the common duct. The gall bladder was removed, the stones were taken from the common duct and the duodenal opening was closed. The patient recovered and appears to be well.

How much pain and suffering could have been saved this woman by removing her gall bladder and its stones twenty years ago!

* * *

Analysis of this series indicates that gallstones, even when silent, are potentially dangerous. Simple, uncomplicated gallstones in good-risk patients can be removed with a low mortality rate. Improving the surgical technic and the preoperative and postoperative care will materially lessen the number of operative deaths. When patients have repeated attacks of gallstone colic, the chances of serious complications are great and operative mortality is high. Early operation soon after the onset of acute cholecystitis is indicated by the basic course of the disease and is warranted by the results; it will reduce the chances of stones' passing into the common duct and avoid the serious complications that follow their presence there and the resultant surgery. The removal of simple, uncomplicated gallstones is an extremely safe procedure and should be urged before the complications of gallstones appear.

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RADIOLOGIC ASPECTS OF GALL-BLADDER DISEASE

MERRILL C. SOSMAN, M.D.*

BOSTON

SINCE the advent of cholecystography in 1924, the diagnosis of gall-bladder disease has become extremely simple and accurate. Its simplicity depends on the limited number of possible diagnoses. Either the x-ray reveals a gall-bladder shadow, or there is no shadow. If there is a shadow, either the gall bladder contains stones or it contains no stones. Occasionally gallstones can be demonstrated in the absence of gall-bladder visualization. In our experience at the Peter Bent Brigham Hospital only 20 per cent of all gallstones are opaque enough to be visible without cholecystography. Compared to the almost infinite number of possible diagnoses in the chest, or the gastrointestinal tract, or even in the bones, the four choices noted above are indeed simple. The variations from normal are few in number, the decision is easy, and the final opinion is frequently categorical, often indubitable.

The accuracy of the x-ray test increases with the attention paid to technical details. One must have good films to make good diagnoses. Nearly all the errors in the radiologic diagnosis of gall-bladder disease can be traced to faults in technic, assuming that the physician who interprets the films has had average experience and possesses good judgment. Under average conditions in any x-ray department doing a considerable amount of diagnostic work, the accuracy of this test approaches 99 per cent. Including borderline cases, in which it is a question of opinion whether the gall bladder is diseased enough to interfere seriously with its function, there is an absolute accuracy of at least 95 per cent. Cholecystography is almost unique in x-ray examinations in that it not only portrays the anatomy of the part under consideration and the consequences of major pathologic reactions but also shows clearly a series of physiologic processes. All other x-ray examinations except one portray anatomic structures and variations caused in them by disease or injury, but little, if any, abnormal physiology. The one exception is intravenous (excretion) urography, and this test is quite similar to cholecystography in concept and execution. The functions of the kidney, however, are so complex and the possibilities of disease, injury and tumor are so numerous that a similar accuracy in diagnosis is not to be expected.

TECHNIC OF CHOLECYSTOGRAPHY

Attention to details and a rigid, precise technic pay large dividends in diagnostic accuracy. Among the first of the important technical factors is adequate equipment — fast apparatus capable of mak-

ing good radiographs in half a second. This helps to avoid blurring of the gall-bladder image by motion, either from breathing, from peristalsis of adjacent organs or from pulsation transmitted to the gall bladder. A fast, thin Bucky diaphragm is also essential to secure good contrast. A cone centered over the gall bladder helps to increase the contrast by excluding other secondary radiations. The tube should be of fine focus to give sharp detail to the image, such as a 2-mm. focal-spot rotating-anode tube, which at the same time allows the use of 300 or 400 milliamperes of current and a correspondingly short exposure. It is most satisfactory to vary the voltage according to the thickness of the patient's abdomen as measured with him prone on the table. The intensifying screens should be clean and free of grain, and as soon as they become abraded or spotted through wear they should be replaced. There is no excuse for some of the dirty, pockmarked screens in daily use in some offices and departments. Contact between the screens and the film should be checked, since lack of close contact results in a blurred image. A target-film distance of 32 to 36 inches instead of the usual 24 to 28 inches helps to improve detail.

Next in importance to the equipment is attention to the details of the test itself. Considering only oral cholecystography at the moment, the dye (tetraiodophenolphthalein) may be administered in any one of several forms or combinations. We originally used the pure dye in enteric-coated capsules, later changing to an emulsion that was mixed with grape juice to disguise both the purple color and the metallic taste. The dye may be dispensed with a weak acid, such as citric, tartaric or malic acid, and simply mixed with water. In an acid medium the dye is precipitated as an insoluble white salt and goes through the stomach unabsorbed. In the alkaline intestinal tract the dye becomes soluble and is absorbed, passing through the portal circulation to the liver, where it is excreted along with the bile salts. It is too dilute when excreted by the liver to cast a shadow on the x-ray films, so that concentration by the gall bladder is essential in demonstrating the gall-bladder shadow. For this reason attempts to show the common duct after cholecystectomy have uniformly failed except by direct injection of opaque material — called "cholangiography" or "choledochography." The common bile duct may be widely dilated after operation and may retain a considerable amount of bile, but never in my experience has it concentrated the liver bile to a point where it could be demonstrated by radiography. A thorough understanding of the

*Clinical professor of roentgenology, Harvard Medical School; roentgenologist, Peter Bent Brigham Hospital

ve steps is essential in interpreting the results of the test.

PREPARATION OF PATIENT AND TECHNIC OF EXAMINATION

Cleansing of the intestinal tract by either catharsis or enema adds to the accuracy of the tests by removing feces, gas or undissolved dye, which may veil or obscure the gall-bladder shadow. A routine catharsis on the day preceding the examination was tried but was soon given up, since it was found that the tetraiodophenolphthalein is in itself cathartic, probably owing to the phenolphthalein portion. Many patients suffer from diarrhea and some from nausea and vomiting as well, but diarrhea has not interfered with a satisfactory visualization of the gall bladder. Obviously, however, if the patient has vomited the dye, enough may have been lost to interfere with the test. This happens particularly in patients with peptic ulcer and those with some degree of pyloric obstruction. Golden² recommends administering 6 cc. of paregoric before the meal that precedes the giving of the dye. This undoubtedly promotes the comfort of the patient and may allow more complete absorption of the chemical. We do not agree with Curl,³ who recommends a high-fat diet for several days before the test to empty the gall bladder. With this procedure there is a larger percentage of unabsorbed precipitated dye remaining in the intestines, particularly when the fat is given during the meal just preceding the administration of the dye. Theoretically this should empty the gall bladder and prepare it ideally for the storage of the bile that contains the dye. Actually it seems to interfere with the absorption of the chemical, perhaps through combination of fatty acids and tetraiodophenolphthalein to form an insoluble compound. Antonucci⁴ recommends a high-carbohydrate intake before cholecystography on the theory that a large glycogen reserve in the liver improves its excretory function. We have had no experience with this preliminary preparation.

The standard procedure, therefore, is to give 3.5 gm. of tetraiodophenolphthalein after a fat-free evening meal, the exact procedure depending on the type of preparation employed. Many hospitals are now using the double-dose technic, giving one dose of 3.0 or 3.5 gm. after a fat-free noon meal and a similar dose after a fat-free evening meal. This has definitely added to the accuracy of the test, with fewer doubtful or faint gall-bladder shadows resulting. After the evening meal and the dose of the dye, the patient should have nothing to eat or drink except water, fruit juice or black coffee until after the x-ray films are taken, usually at 9.00 the following morning. There is no evidence that limitation of fluid intake increases the concentration of the bile as it is excreted from the liver or that increased fluid intake promotes the flow of bile from the liver, so that fluids need not be withheld as in

excretion urography. It is advisable to take a large film of the right abdomen first, at least an 11-by-14-inch film, develop it immediately and view it wet, to locate the gall-bladder shadow. If there is gas or fecal material over the usual gall-bladder area, a cleansing enema — at least 2000 cc. of tap water or normal saline solution — should be used to remove it if it is in the colon, or a drink of water if there is air in the descending duodenum, which may obscure or confuse the findings. The films are best made with the patient prone, the right hand above the head, the face to the right and the right side of the abdomen raised slightly from the table. This position helps to uncover the gall-bladder shadow, particularly in long, thin patients, by rotating the spine slightly to the left and the gall bladder slightly more to the right, rendering the latter less apt to be concealed by the vertebrae. The position of the gall bladder varies tremendously. In the obese or thick-set patient of hypersthenic type it may be at the lateral edge of the liver as high as the tenth rib. In the long, lean hyposthenic patient it may lie over the sacroiliac joint or even reach the brim of the pelvis, and not infrequently it is hidden by the spine unless the position described above is used. In exceptional cases it may be necessary to take films with the patient lying face up, with the body rotated to the right to uncover the gall-bladder shadow either from the spine or from gas in the hepatic flexure. Films in the upright position are occasionally of critical value, as will be shown later. If repeated cleansing enemas are not successful in removing troublesome gas from the gall-bladder area, either the supine technic should be tried or 1 cc. of Pitressin should be given hypodermically, provided there is no contraindication to its use. A satisfactory scout film should include the lower half of the liver shadow and the upper half of the innominate bone, as well as the lumbar spine. In viewing the wet film one should identify the liver edge, the kidney shadow, the iliopsoas shadow and the peritoneal line laterally. Occasionally the overlapping of liver and kidney shadows produces a zone of increased density, which to the uninitiated seems to be the gall-bladder shadow. In 2 routine cases the air-filled fundus of the stomach was recognized in the area where the liver shadow should have been, indicating a situs transversus. In both cases, films of the left upper quadrant demonstrated a normal gall-bladder shadow and averted a serious error in diagnosis. If the shadow is visualized satisfactorily, at least three films are taken, with a cone centered over the area where the gall bladder lies. It has been found advantageous to take these films with slight variation in rotation, and one of them at least at the end of expiration. This often helps one to decide whether overlying shadows, either so-called "positive" or "negative," maintain a constant relation to the gall-bladder shadow, thus aiding in differentiating bubbles of air or

gas and calculi. If these films are technically satisfactory, the patient is given a fat meal, — two eggs, buttered toast and coffee with cream or an eggnog containing two eggs and some cream, — and at least two more films are taken an hour later, using the same position and technic as for the first set of films. If the first films show questionable shadows that may be those of calculi, two films should be taken in the upright position to demonstrate a change in the position of the calculi. Elias, ⁵ in 1932, was the first to show that some gallstones float in the opaque dye-filled bile, whereas most of the calculi sink to the fundus of the gall bladder when the films are made with the patient erect. This was confirmed and amplified by Akerlund. ⁶ The floating phenomenon is an extremely interesting and useful test, frequently changing the final diagnosis from a doubtful to an indubitable one. The stones that float at a given level in the upright position are always the cholesterol or "negative" calculi, and the phenomenon is based on the fact that there is a difference between the specific gravity of the bile in the fundus of the gall bladder, which has been there longest and is therefore the most concentrated, and that of the bile in the neck of the gall bladder, which has come more recently from the liver and is less concentrated and therefore of lower specific gravity. The cholesterol calculi simply seek their own level of specific gravity, and they usually lie in a single horizontal plane, causing a dark streak across the opaque white gall-bladder shadow. ⁷ Frequently the separate calculi are recognizable. It is conceivable that if there were two different kinds of calculi, there would be two separate and distinct horizontal rows in the upright position, but I do not remember having seen this actually demonstrated by x-ray. Nearly all the calculi we see are of the same type or kind in a given gall bladder, and most of the cholesterol calculi were probably laid down in a single shower. Many of them also are seen in gall bladders that concentrate and empty well, so that they must have been made through a physicochemical process at a time when the gall bladder was normal or nearly normal, at least in function. The opaque crystalline pigment calculi also frequently occur in normal gall bladders, but the laminated calculi and those with dense margins around a cholesterol nucleus are oftener found in badly diseased gall bladders, and recurrent infection has probably played a part in their formation. Only the small negative or pure cholesterol calculi float, and the bile must be well concentrated and quite opaque to present this phenomenon. By far the larger majority of calculi, including all the "positive" ones, sink to the fundus of the gall bladder in the upright films, forming a layer of debris at that point. This is just as valuable, however, in identifying them as biliary calculi as is the floating phenomenon across the middle of the opaque gall-bladder shadow.

The films taken an hour after a meal or after the eggnog should also be developed at once and viewed wet before the patient leaves the department. If there has not been at least a 50 per cent decrease in the size of the shadow, further films should be made an hour or two later. The significance of a persistent gall-bladder shadow that does not decrease in size after a meal is discussed below. A proprietary mixture of concentrated lipoids, such as Cholex (National Synthetics Company), is available, and this may be used in place of a fat-containing meal. Its chief advantage is its small bulk and its ease of preparation. It is particularly useful for patients who do not like eggs and for those who are nauseated by the thought of food.

The entire examination as a rule takes only slightly over an hour and requires only two sets of films, as described above — one set fifteen hours after taking the dye and the other at least an hour after the test meal. We originally made several sets of films during the day, ⁸ the patient fasting in the meantime, to demonstrate progressive increase in the density of the shadow as an index of normal concentrating power. After twenty years of experience, we know the expected standard of density at the fifteen-hour examination, and believe that it is unnecessary to prolong the examination beyond the two sets of films, except in case no gall-bladder shadow is demonstrable at the first examination. It has been our custom to check each case of nonvisualization by intravenous injection at a subsequent date. Most roentgenologists, however, prefer to repeat the oral method, and if this is done it is advantageous to do it the following day, the patient being on a fat-free diet the entire time. This obviates hospitalization, which should be done for intravenous injection, and avoids the risks of reaction from the injection, both local and systemic. If any of the dye gets into the tissues around the vein being injected, an intense local reaction is set up. Some patients have had thrombosis of the vein after injection, a few have had acute coronary attacks, and several sudden deaths have been reported after intravenous injection of tetraiodophenolphthalein. Systemic reactions are less apt to occur if the dye is injected slowly — over a period of at least fifteen minutes. Because of these possible reactions many x-ray departments have abandoned the intravenous method entirely and rely on the oral method, using the double dose either routinely or as a check on the single dose if nonvisualization of the gall bladder occurs. In either case a small percentage of patients show a normal gall-bladder shadow at the second examination, when none was seen the first time. This varies from 2 to 10 per cent in different clinics. Many of these shadows are probably the result of errors in technic, either by the patient, who perhaps misunderstood the directions or willfully disregarded them, or by the radiographer, who did not pay attention to the details.

ed above. A careful, conscientious, well-trained technician is an invaluable asset, particularly in this field.

There is a third possibility to be considered — that the gall bladder is visualized but with a shadow darker than normally expected at the given time. In such cases it is wise to repeat the examination, using either the intravenous method — if there is no suspicion of coronary disease — or the double-exposure method. Tracey⁹ strongly advises checking the collateral organic systems — by a gastrointestinal series, a barium enema and so forth — and delaying symptomatic treatment for a short period before rechecking the gall bladder, intimating that there may be physiologic variations that interfere with the test. He states that if the symptoms are relieved by treatment there may be good visualization of a previously faint or nonvisualized gall bladder. Lahey and Jordan¹⁰ go so far as to state that of patients with chronic dyspepsia and nonvisualization of the gall bladder 44 per cent show normal gall-bladder shadows after satisfactory bowel management. Our series has shown no such discrepancy. This is certainly true, however, in the case of jaundice. No harm has followed if the dye is given either intravenously or orally in jaundiced patients, but almost invariably there is nonvisualization of the gall bladder. A good shadow is occasionally obtained when the jaundice is clearing or it is due to hemolysis and not to obstruction. It is much better, however, to wait until the jaundice has entirely cleared before doing a cholecystography. There is no danger in trying it, but it constitutes a waste of time, material and money.

It is of course obvious that if pyloric obstruction or prolonged pylorospasm is present, the dye may be retained in the stomach unabsorbed, in which case nonvisualization obviously results. This complication can be recognized by identifying the finely mottled opaque shadow of the dye in the stomach. In a recent case of this type further gall-bladder films twenty-four hours later revealed passage of all the dye from the stomach and a normal gall-bladder shadow, whereas there was no shadow before. Such a complication may explain the discrepancies noted above between the results reported by Lahey and Jordan and our figures.

Fluoroscopy has not been used routinely in our department since the first days when we were repeating Graham and Cole's experiments,¹¹ and only a few roentgenologists now use fluoroscopy as part of cholecystography. We found it to be of no help in the clinical examination, and now use it only in an occasional patient when spot films in the upright position are desired. Good films give much more information, especially concerning detail, than can be expected from fluoroscopy. The information obtained by fluoroscopy about changes in shape and in position with palpation and change in posture is

not of enough importance to justify the time consumed by the method.

Recently a new drug has been found that also renders the gall bladder opaque some hours after ingestion. This substance is in no way related to tetraiodophenolphthalein, and it is less apt to cause some of the uncomfortable side effects such as nausea, vomiting and diarrhea. Originally described in Germany as "Biliselectan,"¹² it is *beta*-(4-hydroxy-3,5-diiodophenyl)-*alpha*-phenyl-propionic acid. It is dispensed as a 0.5-gm. tablet, and is taken by mouth with sips of water, lemonade or weak tea after a fat-free evening meal, just as in the oral method with tetraiodophenolphthalein. So far, after use in about 150 patients, it has shown several distinct advantages over tetraiodophenolphthalein. There is definitely less toxic reaction, such as nausea, vomiting and diarrhea, in the gastrointestinal tract, and there is usually little if any opaque residue in the bowel to obscure the gall-bladder area. The drug is excreted largely through the kidneys, and a few patients complain of mild burning on urination the morning after taking the tablets. In this country it is manufactured by the Schering Corporation under the trade name of Priodax and by the National Synthetics Company as Dikol. We have been using it routinely since preliminary clinical tests demonstrated its advantages. The standard dose is 3.0 gm. (six tablets). Double doses have frequently been given without untoward results and with excellent visualization of the gall bladder at fifteen hours, with as dense a shadow as any seen following intravenous administration of tetraiodophenolphthalein. In fact, the shadow is often so opaque that small stones may be entirely hidden. This chemical has not been accepted for intravenous injection. It will probably replace the various forms of tetraiodophenolphthalein preparations in most x-ray departments for oral use.

INTERPRETATION OF RESULTS

The facts that may be demonstrated by cholecystography are the size, shape and position of the gall bladder, the degree of filling and the relative concentration, the presence or absence of shadows indicative of calculi and the amount of emptying, as revealed by a decrease in size, usually one hour after a fat-containing meal.

The size, shape and position of the gall bladder are extremely variable. A small gall bladder, if of normal density, does not indicate inability to fill normally; rather it suggests that the patient has partaken of forbidden food. A large gall bladder is of no clinical importance unless there is lack of concentrating power or other evidence of disease. A markedly distended gall bladder, if due to obstruction anywhere in the biliary tract, either fails to fill with the dye or does not concentrate it. A gall-bladder shadow of normal density for the given

method should therefore be considered normal regardless of its size, if the other findings are also normal. The position of the gall bladder depends on the habitus of the patient, as noted above. Changes in position alone are of no value in interpretation, unless the cause of displacement can be demonstrated. Situs inversus should always be kept in mind because of the possible error in interpretation as a case of nonvisualization. Changes in shape, however, are occasionally important, usually as an indication of fixation or adhesions by extrinsic disease. In actual practice this is rare unless there is a history of surgical drainage of the gall bladder. Most of the dense adhesions found at operation cannot be demonstrated or even suspected by x-ray examination. It must be remembered that one is viewing a three-dimensional object in only two dimensions and that any abnormal or peculiar shape must be interpreted accordingly. The fundus of the gall bladder is frequently seen partly overlapping the body of the shadow. This is as a rule not due to adhesions but to the free portion's folding over the portion that is normally fixed to the undersurface of the liver. Rarely the gall bladder is more or less divided into two or three compartments by either transverse or oblique bands. These may be either partial septums in the wall of the gall bladder — usually in the mucosal layer — or bands compressing it extrinsically. In either case, the finding is of little or no importance per se. Such gall bladders usually fill, concentrate and empty to a normal degree, and the few patients in this series that have been operated on without other indications have not had their symptoms relieved by cholecystectomy.

The filling of the gall bladder with dye-laden bile obviously depends on its ability to empty. If it cannot empty, there is poor filling and a faint shadow or no filling with fresh bile and no shadow. In either case the interpretation is based on the density of the shadow and is inseparable as a fact from the observations based on lack of concentration. If there is no visualization of the gall bladder by opaque material, the logical and correct interpretation is a nonfunctioning gall bladder.*

If the radiographic technic has been above criticism and the patient has faithfully followed directions, this is a very reliable finding. In 90 per cent of nonvisualized gall bladders in our series gallstones have been found at operation. The accuracy of this finding alone is close to 99 per cent, in terms of grossly pathologic gall bladders, particularly if the examination has been repeated either by intravenous injection or by the double-dose technic and the find-

ing has been verified. Much less reliable, however, has been the demonstration of a poorly functioning gall bladder or a faint shadow, particularly by the single-dose oral method. Gross pathologic changes were found at operation in only 75 per cent of those in this group who came to operation. A cholecystographic examination giving this finding without calculi should of course be repeated, preferably by intravenous injection, so that all question of failure of absorption of the dye can be eliminated. So far we have found fewer errors in this group with Pridax, particularly with the double-dose technic. If the symptoms are not characteristic or acute, it may be wise to delay the second examination for several weeks, as Tracey⁹ suggests. On the whole, if a shadow of fair to good density results, no calculi are found and the gall bladder empties promptly and well, it is safer to class the result as within the normal range rather than to try to estimate the shadows of fair density in terms of moderate degrees of cholecystitis.

It should be noted that our results are not based on histologic examination of the excised gall bladder alone. Autopsies have shown that 60 per cent of people over forty years of age have noncalculous cholecystitis, but mostly of mild degree and of doubtful significance as regards the production of distressing symptoms.¹³ Most if not all of this mild cholecystitis would be classed by us as no more than normally expected, and if no gall-bladder shadow were obtained in such a patient we should consider it an error rather than a success.

The radiographic demonstration of calculi, however, is the most reliable finding of all, and the most significant to the patient, the physician and the surgeon. In our series this finding in patients coming to operation has been accurate in over 99 per cent and there have been several years when it has been 100 per cent correct. Many patients in whom gallstones have been reported do not have the finding either verified or disproved, and this leaves a possible source of error, since they are apt to be the ones with milder symptoms. If the x-ray films are of excellent quality and if calculi, either positive or negative, are demonstrated, there should be no more than a 1 per cent chance of error. The causes of these errors are discussed below. It must be emphasized, however, that not all gallstones can be visualized, since there are many cases of calculous cholecystitis in the cases with nonvisualized gall bladders in which the calculi are not radiopaque. Of all the cases coming to operation in which gallstones were found, calculi were positively reported in only 75 per cent. The others not identified preoperatively, however, were reported as nonfunctioning or pathologic gall bladders, and as noted above we have learned that 9 out of 10 patients in this group are found at operation or autopsy to have biliary calculi. The routine films taken one hour after the meal have been helpful in securing this

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It must be emphasized that x-ray examination of the gall bladder, or of any organ of the body, does not explain symptoms. Gallstones may be silent for long periods of time. The demonstration of calculi in the gall bladder is a factual finding, but their relation to the patient's symptoms is quite another problem, and if there is a discrepancy the referring physician should have the other organs or systems investigated.

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Some of the possible errors have already been pointed out. Another source of error is in reality due to a failure of the test, since it has been shown that a moderate degree of chronic cholecystitis or even an acute cholecystitis is compatible with normal function and a normal cholecystographic shadow. Cholesterosis, or so-called "strawberry gall bladder," may be present and not interfere with gall-bladder function as demonstrated by this test. Several times, however, we have noted a fine irregularity in outline of a normally opaque shadow, due to diffuse cholesterosis of the mucosa of the gall bladder but not interfering with its function. Gas, either in the colon or in the descending duodenum, has been the greatest cause of error. Either the stones were hidden or obscured by overlying gas or a persistent bubble of gas was interpreted as a calculus. Motion due to breathing during the exposure is another frequent source of error, since it may blur out the shadows of calculi. This is a particularly important factor in large charity hospitals and teaching clinics, in which many patients do not speak or understand the English language. It is a constant source of wonder that many people do not know how to hold their breath even for one

method should therefore be considered normal regardless of its size, if the other findings are also normal. The position of the gall bladder depends on the habitus of the patient, as noted above. Changes in position alone are of no value in interpretation, unless the cause of displacement can be demonstrated. Situs inversus should always be kept in mind because of the possible error in interpretation as a case of nonvisualization. Changes in shape, however, are occasionally important, usually as an indication of fixation or adhesions by extrinsic disease. In actual practice this is rare unless there is a history of surgical drainage of the gall bladder. Most of the dense adhesions found at operation cannot be demonstrated or even suspected by x-ray examination. It must be remembered that one is viewing a three-dimensional object in only two dimensions and that any abnormal or peculiar shape must be interpreted accordingly. The fundus of the gall bladder is frequently seen partly overlapping the body of the shadow. This is as a rule not due to adhesions but to the free portion's folding over the portion that is normally fixed to the undersurface of the liver. Rarely the gall bladder is more or less divided into two or three compartments by either transverse or oblique bands. These may be either partial septums in the wall of the gall bladder — usually in the mucosal layer — or bands compressing it extrinsically. In either case, the finding is of little or no importance per se. Such gall bladders usually fill, concentrate and empty to a normal degree, and the few patients in this series that have been operated on without other indications have not had their symptoms relieved by cholecystectomy.

The filling of the gall bladder with dye-laden bile obviously depends on its ability to empty. If it cannot empty, there is poor filling and a faint shadow or no filling with fresh bile and no shadow. In either case the interpretation is based on the density of the shadow and is inseparable as a fact from the observations based on lack of concentration. If there is no visualization of the gall bladder by opaque material, the logical and correct interpretation is a nonfunctioning gall bladder.*

If the radiographic technic has been above criticism and the patient has faithfully followed directions, this is a very reliable finding. In 90 per cent of nonvisualized gall bladders in our series gallstones have been found at operation. The accuracy of this finding alone is close to 99 per cent, in terms of grossly pathologic gall bladders, particularly if the examination has been repeated either by intravenous injection or by the double-dose technic and the find-

ing has been verified. Much less reliable, however, has been the demonstration of a poorly functioning gall bladder or a faint shadow, particularly by the single-dose oral method. Gross pathologic changes were found at operation in only 75 per cent of those in this group who came to operation. A cholecystographic examination giving this finding without calculi should of course be repeated, preferably by intravenous injection, so that all question of failure of absorption of the dye can be eliminated. So far we have found fewer errors in this group with Pridax, particularly with the double-dose technic. If the symptoms are not characteristic or acute, it may be wise to delay the second examination for several weeks, as Tracey⁹ suggests. On the whole if a shadow of fair to good density results, no calculi are found and the gall bladder empties promptly and well, it is safer to class the result as within the normal range rather than to try to estimate the shadows of fair density in terms of moderate degrees of cholecystitis.

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The presence of cholecystitis in either an acute or a mild chronic stage and with a normal gall-bladder shadow has already been mentioned as an error in diagnosis. The clinical importance of a so-called "mild chronic cholecystitis" is doubtful. If these cases are excluded, there will be a high accuracy in the confirmed diagnosis of normal gall bladder, although it is hardly fair to accept the

diagnosis as confirmed if the gall bladder is removed. Small gallstones may be missed by palpation alone during operation.

Occasionally small stones or gritty particles like sand are found in the gall bladder at operation when the shadow appeared quite normal. This was quite rare in our experience. Others have reported the finding in 5 per cent of cholecystographically normal gall bladders. The more attention is paid to technical details, the smaller this percentage will be, particularly if upright films are taken routinely, as is now being done in some clinics.

Before cholecystography was announced by Graham and Cole,¹¹ much emphasis was placed on the so-called "indirect signs" of gall-bladder disease. A presumptive diagnosis of gall-bladder disease was often made, based on slight deformities of the duodenal bulb, pressure effects on the duodenum, irritability of the duodenal cap and pylorospasm, any of these signs alone. As now known, these alleged diagnoses were mostly guesswork, and little if any attention is now paid to these minor physiologic or anatomic changes when considering gall-bladder disease. Only rarely does the diseased gall bladder cause deformity of the duodenal cap, and the diagnosis of adhesions from the gall bladder extremely infrequent. Occasionally, however, it can be made accurately and logically, particularly when there is a fistula between the duodenum and the biliary tract. This occurs oftenest as the result of ulceration of a stone or stones from the gall bladder into the duodenum, less often by perforation of a duodenal ulcer into the common bile duct and even less frequently as the result of a carcinoma of the papilla with incompetence of the sphincter of Oddi. The rupture of gallstones into the duodenum occurs most frequently in old women, and if the stone is large enough, it may cause obstruction of the small bowel, usually near the ileocecal valve. Gallstone ileus can be promptly diagnosed by demonstrating the calculus in the obstructed small bowel, by noting air or gas in the gall bladder or biliary tract or by demonstrating the fistulous connection with barium. Films of the abdomen taken for intestinal obstruction or acute abdominal symptoms should always include at least the lower half of the liver, and the roentgenologist should always look for air in the common or hepatic ducts. One sees only what one looks for, and it is wise to train oneself to look for streaks of air in the liver shadow. The disappearance of calculi, particularly large calculi, previously known to have been in the gall bladder is presumptive evidence of perforation or rupture of the gall bladder. Smaller calculi may be passed into the duodenum through the intact cystic and common ducts. This may account for an occasional error in diagnosis when gallstones demonstrated by x-ray are not found at operation, particularly if the operation is done some time after the x-ray examination. The passage of calculi from the

gall bladder directly into the duodenum is probably more frequent than statistics indicate, since we usually see several cases a year. Frequently the stones are passed uneventfully in the stools. Occasionally they are vomited — a dramatic method of demonstrating gallstones. The fistulas may heal spontaneously, whereas with others there is a prolonged period of intermittent chills and fever, frequently without jaundice. Rarely if ever can a normal gall-bladder shadow be found by cholecystography after such a spontaneous perforation, but cases have been reported in which subsequent crops of gallstones have formed.

There is one condition in which an erroneous diagnosis of gallstone ileus is sometimes made. There may be concretions or calculi in the appendix that exactly simulate gallstones — laminated, faceted ring shadows that are in reality appendicoliths. If there is an associated ileus from acute appendicitis or peritonitis, the calculi may be interpreted as being in the terminal ileum and as causing obstruction of the small bowel. There is no air in the biliary system, however, in such a case, and that should put one on his guard.

Fistulas from the gall bladder may also lead to the stomach, to the colon, to other parts of the small bowel and even through the diaphragm into a bronchus. In any case with biliary fistula the gall bladder cannot be visualized by cholecystography, but on rare occasions it can be visualized by a barium meal or by a barium enema.

The direct demonstration of opaque or positive gallstones by x-ray films without cholecystography is quite reliable and rarely needs to be confirmed by the Graham test. Occasionally renal calculi simulate the typical ring shadows or faceted appearance of gallstones, particularly if they are formed in a hydronephrotic, pyonephrotic or polycystic kidney. Oblique films, lateral films or those made in different phases of respiration usually suffice to differentiate them. Occasionally it is necessary to do both cholecystograms and pyelograms to be sure where the calculi are located. Calcified lymph nodes are occasionally mistaken for gallstones, but fortunately they are rare in the gall-bladder area. Biliary-pigment calculi may look very much like calcified nodes, so that the reverse error is also possible, and has been made. When the cystic duct is completely obstructed, the gall-bladder mucosa may excrete calcium into the bile¹⁹ and form milk-of-calcium bile, which may exactly simulate a normally dense gall-bladder shadow. It may form a calcified cast of the gall bladder, or the calcium may be deposited in the wall of the gall bladder. These complications can be recognized by plain films of the gall-bladder area before cholecystography.

Cholangiography is a valuable method of examination when stones in the common bile duct are suspected. If it is done during operation, using a portable x-ray apparatus, it is classed as "immedi-

ate";²⁰ if it is done several days or more after operation, it is spoken of as "delayed."²¹ The latter is much to be preferred, since it can be done under fluoroscopic observation and control, with spot films as indicated. The size, shape, location and direction of the common duct and hepatic duct can be demonstrated, obstructions located, patency determined and emptying into the duodenum observed. We prefer to use lipiodol or Iodochloral, but Thorotrast or Diodrast can be successfully employed. The opaque material is injected slowly through the drainage tube or T tube, using very gentle pressure, and its progress is carefully watched on the fluoroscopic screen. If an obstruction or a filling defect is encountered, spot films are made at once, since small calculi or debris may be covered up by too much opaque material. It is not always possible to differentiate calculi in the common duct and bubbles of air or small blood clots. In the latter case re-examination several days later may give perfectly normal results. Not infrequently one or more of the pancreatic ducts are visualized if they empty into the common duct. Cholangiography is probably of the greatest usefulness when there is a question whether it is safe to remove the drainage tube. It is invaluable and essential when such operations as reconstruction of the common bile duct have to be done.

SUMMARY

Cholecystography is a simple, safe and extremely accurate method for the study of the gall bladder.

Good films are necessary if good diagnoses are to be made. Films of exceptional quality give the greatest accuracy. The utmost attention to technical detail pays dividends in diagnostic correctness.

The positive diagnosis of gallstones or of a non-functioning gall bladder should be correct in 99 per cent of the cases.

A new chemical (Priodax), not related to tetraiodophenolphthalein, has been tried successfully and is thought to be superior in routine oral examinations of the gall bladder to chemicals previously used.

The details of radiographic technic and the principles of roentgenologic interpretation are discussed.

721 Huntington Avenue

REFERENCES

Between February, 1924, when Graham and Cole's original article appeared, and September 30, 1943, eight hundred and sixty-four articles on cholecystography have been listed in the *Cumulative Index*. It is impossible and unnecessary to list them all, so that only the ones referred to in this article are subjoined. Many important and valuable papers are omitted, and their lack of inclusion does not reflect on their value.

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diagnosis as confirmed if the gall bladder is not removed. Small gallstones may be missed by palpation alone during operation.

Occasionally small stones or gritty particles like sand are found in the gall bladder at operation when the shadow appeared quite normal. This was quite rare in our experience. Others have reported this finding in 5 per cent of cholecystographically normal gall bladders. The more attention is paid to technical details, the smaller this percentage will be, particularly if upright films are taken routinely, as is now being done in some clinics.

Before cholecystography was announced by Graham and Cole,¹¹ much emphasis was placed on the so-called "indirect signs" of gall-bladder disease. A presumptive diagnosis of gall-bladder disease was often made, based on slight deformities of the duodenal bulb, pressure effects on the duodenum, irritability of the duodenal cap and pylorospasm, or any of these signs alone. As now known, these alleged diagnoses were mostly guesswork, and little if any attention is now paid to these minor physiologic or anatomic changes when considering gall bladder disease. Only rarely does the diseased gall bladder cause deformity of the duodenal cap, and the diagnosis of adhesions from the gall bladder is extremely infrequent. Occasionally, however, it can be made accurately and logically, particularly when there is a fistula between the duodenum and the biliary tract. This occurs oftenest as the result of ulceration of a stone or stones from the gall bladder into the duodenum, less often by perforation of a duodenal ulcer into the common bile duct and even less frequently as the result of a carcinoma of the papilla with incompetence of the sphincter of Oddi. The rupture of gallstones into the duodenum occurs most frequently in old women, and if the stone is large enough, it may cause obstruction of the small bowel, usually near the ileocecal valve. Gallstone ileus can be promptly diagnosed by demonstrating the calculus in the obstructed small bowel, by noting air or gas in the gall bladder or biliary tract or by demonstrating the fistulous connection with barium. Films of the abdomen taken for intestinal obstruction or acute abdominal symptoms should always include at least the lower half of the liver, and the roentgenologist should always look for air in the common or hepatic ducts. One sees only what one looks for, and it is wise to train oneself to look for streaks of air in the liver shadow. The disappearance of calculi, particularly large calculi, previously known to have been in the gall bladder is presumptive evidence of perforation or rupture of the gall bladder. Smaller calculi may be passed into the duodenum through the intact cystic and common ducts. This may account for an occasional error in diagnosis when gallstones demonstrated by x-ray are not found at operation, particularly if the operation is done some time after the x-ray examination. The passage of calculi from the

MEDICAL PROGRESS

ENDOCRINE ASPECTS OF CANCER (Concluded)*

IRA T. NATHANSON, M.D.†

BOSTON

CLINICAL OBSERVATIONS

Tumors of Breast

Carcinoma of breast. The peak of age incidence in 2165 cases of cancer of the breast at the onset was about forty-seven years.¹²² The median age was fifty-two years, that is, as many cases occurred before that age as after it. Approximately a third of the patients were under forty-five years of age, another third from forty-five to fifty-five, and the remainder older than fifty-five. Taylor¹²³ found that about one third of the cases occurred during the period of mature ovarian function, another third appeared five years before and after the menopause and the remainder in women whose ovarian function had ceased five years or more. Thus, the two studies are in agreement but it must be pointed out that susceptibility to cancer of the breast steadily increases with age.¹²² Further data on the relation of breast cancer to the menopause were supplied by Olch.¹²⁴ According to his studies 72 per cent of normal women pass through the menopause from forty to fifty years of age, whereas 55 per cent of those with cancer are still menstruating at the age of fifty. It was concluded that almost five times as many women with breast cancer had a delayed menopause as compared with normal women. Data on the length of the menopause are not readily available. This may be of importance for, even though amenorrhea is one of the primary signs of the climacteric, the ovary may continue to be active and secrete estrogens for a relatively long period.¹²⁵ Since corpus-luteum function is usually diminished or absent during the menopausal years, the normal cyclic change disappears and estrogen stimulation may continue unopposed. Cancer of the breast may appear many years after castration, even when the latter has been performed at an early age. Estrogens presumably of adrenal origin are still recovered from the urine of patients who have been castrated, as well as from the urine of postmenopausal women.¹²⁵ Herrell¹²⁶ reviewed the records of a large number of patients in the same age group with and without cancer of the breast. The findings disclosed that in the cancer group the incidence of complete

ovariectomy before the tumor appeared was 1.5 per cent. The incidence in the noncancer group was 15.4 per cent, or ten times as great.

It is not known whether women who develop breast cancer have a higher percentage of menstrual disturbances than those who are free of the disease.¹²⁷ In one study, however, it was found that the menstrual pattern changed shortly before the discovery of the disease.¹²³ So far as can be determined there is no gross effect of the menstrual cycle on the primary tumor. The rapidity of growth of the primary tumor during pregnancy¹²⁸ and the appearance of a tumor in the second breast during another pregnancy,¹²⁹ which may ensue subsequent to treatment of the first lesion, is well recognized. Changes during lactation are usually more striking.¹²³ Whether these effects are caused by hormones elaborated in pregnancy or lactation or to the generalized metabolic changes has not been established.¹³⁰

Breast disease in general is frequently associated with disease or abnormalities of the uterus and ovaries, and in this respect cancer of the breast is no exception.^{123, 127} For example, Taylor¹³¹ found that cancer of the breast and endometrium may arise in the same patient. This information suggests that the entire reproductive system may be subject to the same abnormal stimulus. Nulliparous women have a higher incidence of cancer of the breast than those who have borne children.¹³² This appears to be the reverse of the situation in the mouse. Some believe that early weaning of the child or faulty lactation conduces to the development of breast cancer, in that they result in stasis and breakdown products which may cause chronic irritation.^{133, 134} A study of 350 children of women with breast cancer revealed that 72 per cent were nursed for at least six months and of the remainder, a small number were deliberately weaned or not nursed because of inadequate milk supply.¹²³ Further studies of lactation are indicated, since there is a possibility of an abnormal physiologic state that in itself predisposes to cancer.

The significance of a relation between certain types of chronic cystic mastitis and cancer is a subject of much controversy. Warren's¹³⁵ studies, which were confirmed by Logie,¹³⁶ demonstrate that the attack rate of breast cancer for women with chronic cystic mastitis in the premenopausal group (thirty to forty-nine years of age) was nearly twelve times greater than that of the general female population in the same period. After the age of fifty it

*From the Medical Laboratories of the Collis P. Huntington Memorial Hospital, Harvard University, the Tumor Clinic of the Massachusetts General Hospital and the Pondville Hospital, Walpole, Massachusetts (Massachusetts Cancer Commission, Harvard University).
†Instructor in surgery, Harvard Medical School; assistant in surgery, Massachusetts General Hospital; assistant surgeon, Pondville Hospital.

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LABORATORY NOTE

A SIMPLE TECHNIC FOR RAPID SECTIONING

H. EDWARD MACMAHON, M.D.,* AND SHIRLEY B. DELVECHO†

CAMBRIDGE, MASSACHUSETTS

IN SELECTED cases the value of an immediate diagnosis at the operating table cannot be over-emphasized. The methods of obtaining this information vary. The usual procedure is to freeze tissue, cut a section with a microtome, stain it by dipping in staining solution, rinse it in water and mount it in water or gelatin. There are many minor modifications of this, which is not to be wondered at since the preparation of such sections is still customarily carried out by the pathologist rather than by his technician, and since each pathologist has adopted his own way of handling, cutting and staining tissues. Yet all these technics appear to rely on a microtome, a sharp microtome knife, a tank of carbon dioxide, a bottle of staining solution, glass rods, picks, brushes, staining dishes, rinsing dishes, filter paper, funnels, slides, coverslips and towels. Added to this list, in the case of the peripatetic pathologist, is an assortment of wrenches, wooden blocks and washers, and last but not least a stout, reinforced bag for carrying this equipment.

The following method has been successfully tried over a period of a year, and because of its simplicity it has a particular application to the work of the pathologist in the field. The procedure is so quick and so accurate that it warrants a trial. If one wishes to carry out the usual freezing technic as well, no time is lost, for the method here described can be completed during the few seconds that elapse while the tissue is being frozen for sectioning. It is quite inexpensive, for it eliminates the microtome, microtome knife, carbon dioxide, staining

solution and practically all the paraphernalia that have just been enumerated. The basis of this method is the staining of a thin layer of fresh, unfixed and unfrozen tissue, with a stain that, instead of being preserved as a liquid, is kept as a thin, dry film over the surface of an ordinary glass slide.

Some difficulty was encountered in obtaining thin even films, but this has been overcome by coating one surface of the slide with Mayer's albumen-glycerin mixture, a space being left at one end of the slide for handling, and dipping it for a few seconds in the staining solution—a 1 per cent aqueous solution of toluidine blue. The slide is then drained, the reverse side is wiped free of stain, and to ensure a uniformly stained surface the slide is left on a flat surface until dry. Several slides can be prepared at one time and kept indefinitely; they are always ready for use.

The only equipment required is a safety-razor blade, a prepared stained slide, a clean slide and a clean coverslip—all of which can be carried in a vest pocket. The technic is as follows:

- Cut a thin section that can be easily handled.
- Holding the section on the blade, gently place it on the ball of a finger.
- Draw the stained slide lightly and quickly across the section, staining only one surface of the tissue.
- Immerse the tissue in water.
- Mount the tissue on a glass slide with the stained surface up.
- Place a coverslip over the section, and with a good light examine the tissue.

The results of this technic have been as good as, if not better than, those obtained by the longer and more complicated procedures. It has been tried on breast tissue, lymph nodes, endometrial curettings, cervical tissue and fragments of rectal mucosa. During the trial period the accepted freezing method was used at the same time in each case, and as is the custom, permanent sections were ultimately prepared. In no case did the frozen-section or final report conflict with the original rapid-section diagnosis.

330 Mount Auburn Street

*Pathologist, Cambridge Hospital.
†Technician, Cambridge Hospital.

are as yet equivocal.¹²⁷ Observations suggest that the origin of fibroadenomas may be explained partially on the basis of endocrine dysfunction. It is also possible that they arise as a result of atypical stimulation, especially since they usually occur when the metabolism and secretion of the sex hormones are at their height and may be abnormal.

Tumors of Uterus

Cancer of cervix. Cancers of the cervix arise more frequently in multiparous women than those who have not borne children. Hofbauer¹⁵⁴ advanced the theory that the increased incidence of cancer of the cervix in this group resulted from intensive hormone stimulation during pregnancy rather than from birth injuries. The median age of cancer of the cervix is about forty-nine years.¹⁵⁵ It is not infrequent to find the disease in women passing through the menopause, when the symptoms may be attributed to the climacteric syndrome. Cancer of the cervix is occasionally associated with cancer of the breast and myomas of the uterus but less so than is carcinoma of the endometrium.¹⁵⁶ In our clinics, 3 women have developed metaplasia of the cervical epithelium after estrogen administration. The lesions regressed after treatment was discontinued in two patients, but in the third case an early cancer was diagnosed, which was subsequently confirmed by hysterectomy. Other observers have reported the development of cervical cancer in 3 of 43 patients treated by estrogens for senile vaginitis.¹⁵⁷ Yet other investigators failed to find such lesions after treating over 200 women with estrogens over periods varying from a half to five and a half years.¹⁵⁸ Hence, at the present time, the relation of these cancers to the estrogenic hormone is equivocal. In a considerable number of cases, cervical polyps have developed after estrogen administration to postmenopausal women. Hormone excretion studies to date are few, and no conclusions can be drawn from them.¹⁵⁶

Hyperplasia of endometrium. This lesion can be produced with comparative ease, especially in the absence of the ovaries in animals^{62, 64, 69} and in women,¹⁵⁹ particularly after the menopause. It arises spontaneously at the menopause in patients in whom ovulation is apparently deficient and in the presence of granulosa-cell or thecal-cell tumors of the ovary. These tumors frequently give rise to elevated titers of estrogenic hormone in the urine. Most investigators are of the opinion that the lesion is caused by continuous stimulation by estrogens that is unopposed by hormones possessing a balancing effect, such as the corpus luteum.¹⁵⁶ These assumptions are based on studies on patients in whom persistent large unruptured follicles have been found in the absence of a recent corpus luteum.¹⁶⁰ The histologic changes vary from a proliferation of the endometrium to those simulating early adenocarcinoma.¹⁵⁶ The fact that these

effects may be reversed by treatment with androgens and progesterone¹⁶¹ or following castration by either radiation or surgery further incriminates estrogens as the initiating factor. According to Taylor,¹⁵⁶ the origin of cystic hyperplasia of the human endometrium as a result of unopposed stimulation with estrogens on the basis of ovarian dysfunction may be regarded as established. He further points out that the finding of endometrial hyperplasia in conjunction with a tumor of the reproductive tract is presumptive evidence that estrogens are of some significance in the origin of the neoplasm as well. Regarding endometrial hyperplasia arising in the years after the menopause, the explanation is more difficult. As already pointed out, the estrogenic hormone may be found in varying amounts in the urine long after the menopause. Excretion studies of urinary estrogenic hormone suggest an increased urinary output, but these need confirmation.¹⁵⁶

Cancer of endometrium. This type of cancer is less frequent and usually occurs later in life than cancer of the cervix, suggesting that it may arise on a relatively senile endometrium. The median age in 331 cases was sixty-one.¹⁵⁵ According to statistical studies the disease is somewhat more frequent in nulliparous women and in those with a delayed menopause.¹⁶² Several cancers of the endometrium have apparently arisen after long-continued administration of estrogens.¹⁶³ This may very well be coincidence since it seems likely that more cases would have come to attention considering the sensitivity of the endometrium to the hormone at any age. Nevertheless there are now a fair number of cases reported in which endometrial cancer has been found in association with granulosa-cell tumors of the ovary. Taylor¹⁵⁶ points out that, in view of the rarity of these ovarian tumors, it is hardly conceivable that the associated endometrial lesion was merely coincidence. He states, therefore, that in these particular cases it is difficult to deny the sequence of increased estrogen stimulation, hyperplasia of the senile endometrium and, finally, cancer. Since endometrial hyperplasia is part of the picture, it is of interest to investigate the significance of this lesion as a precancerous change. Endometrial hyperplasia is fairly frequent, but endometrial carcinoma is relatively rare, and although some believe that hyperplastic changes are a predisposing factor, long-term studies of these cases have shown that few patients eventually develop cancer.¹⁵⁶ Furthermore, even though cancer is sometimes found arising in association with endometrial hyperplasia, some are of the opinion that such an occurrence is purely accidental. This is discussed in some detail by Taylor.¹⁵⁶ It must be remembered, however, that as in the case of the relation of chronic cystic mastitis to cancer of the breast, agreement concerning the histologic criteria is of importance. Finally, it is of interest to point

was two and five-tenths times as great, and for the entire group four and five-tenths times higher, suggesting that cancer may occur in association with or superimposed on the benign lesions during the period of greatest ovarian function.

Many have used castration as an adjunct to the treatment of cancer of the breast. This procedure is based on the work of Beatson,¹³⁷ who noted alleviation of signs and symptoms following castration in several women with cancer of the breast. Of late, x-ray therapy has usually been substituted for surgical extirpation of the ovaries.¹³⁸ The castration is of most value in premenopausal patients, although the effects are temporary, and seems to be of little benefit in the postmenopausal group. Bone metastases, as judged by x-ray examination, seem to regress partially or to disappear completely for a time. Relief from pain is frequently noted.¹²⁷ Effects on the primary tumor or lymph-node metastases are slight. It has been concluded that castration may be expected to result in temporary relief in about one third of the patients with extensive disease.¹³⁹ It cannot be demonstrated as *definitely advantageous when employed as a prophylactic procedure in patients submitted to the radical operation.* A report by Farrow and Adair¹⁴⁰ and an unpublished observation¹⁴¹ revealed similar changes in the osseous metastases and in the relief of pain after orchidectomy in males with cancer of the breast. In many cases, laboratory evidence reveals discrepancies regarding the efficacy of x-ray castration as compared to surgical removal of the ovaries.¹²⁵ X-ray was adequate in some cases, as judged by the urinary estrogen excretion, but in others fluctuations in the output appeared even though the patients became amenorrheic. Hence, it is essential that, if castration by x-ray is to be used effectively, factors such as the age of the patient and the size of the portal are important in determining an adequate dosage.

Three reports have appeared on the possible development of cancer of the breast in women after prolonged administration with estrogens.¹⁴²⁻¹⁴⁴ I know of at least 2 cases that have been associated with prolonged and intensive estrogen therapy. There is a good possibility that these were merely coincidental, but it certainly must be considered that the estrogens may have been contributory.

Attempts have been made to influence the course of cancer by the administration of hormones.¹⁴⁵ In our clinics, thus far, we have been unable to demonstrate a direct effect regarding augmentation or inhibition of the growth of the primary tumor by the injection of either estrogens or androgens. Farrow and Woodard¹⁴⁶ have noted that in the premenopausal group, skeletal metastases are apt to occur early. They also reported a marked acceleration of osseous metastases after intensive estrogen or androgen therapy. These changes were accompanied by an increased bone absorption and ele-

vations in the serum and urinary calcium levels. Several cases in our clinics treated in a like fashion showed the same changes. In the past few years, however, reports have appeared concerning beneficial effects following prolonged androgen^{147,148} and estrogen therapy^{149, 150} in cancer of the breast. Many of the cases treated with the estrogenic hormone were given x-ray therapy in addition, and the effects of the latter were considered to be enhanced by the hormone treatment. These reports of a satisfactory response to hormone therapy are exceedingly difficult to evaluate at present, because in some cases factors such as complete histories and histologic confirmation of the disease are lacking. Until these methods of therapy receive further trial under carefully controlled conditions in large clinics, the subject must be left entirely open.

Excretion studies of the hormones with the present methods have failed to yield much information.¹²⁷ Several conclusions, however, may be drawn from such investigations: there is no significant deviation in the excretion of sex hormones in women with breast cancer: there is no proof that sex hormones are not involved in the disease or that abnormal secretion of the hormones does not accompany or precede the development of breast cancer—it is significant that normal excretion rates may be found in the presence of breast cancer; and cancer of the breast may be independent of hormonal influence once it develops.

The available evidence from all sources leads one to conclude that definite proof for the hormones as the direct cause of cancer is lacking. It is possible that in some cases they may be indirectly responsible by producing a fertile soil for the disease to develop.

Fibroadenoma of breast. These tumors seldom arise before puberty or after the menopause. Generally they are detected in the second and third decades. The lesions are usually slowly growing, and although they may pass unnoticed for a long time, it is possible that they arise in the early years after the menarche, when atypical menstrual activity is not infrequent. The disease is said to occur oftener in persons of a definite constitutional type, namely, nulliparous women with a relative underdevelopment of the pelvic organs and breasts.¹²³ The menstrual cycles are seldom abnormal when the patients are first seen, although some give a history of a period of abnormal cycles following the menarche.¹²⁷ Definite changes have been observed, however, in the size and the histologic appearance of the tumors during the menstrual cycle¹⁵¹ and during pregnancy and lactation.^{152, 153} Estrogens have been given over a long period to patients in the presence of and following the removal of fibroadenomas.¹²⁷ No new tumors have been observed that could be attributed to the hormone, since additional lesions frequently arise spontaneously. The significance of excretion studies of the sex hormones

seems to be directly related to the secretory activity of the gland.¹⁸⁴ Serum-acid phosphatase levels are frequently elevated in patients with cancer of the prostate, particularly those with bone metastases.^{182, 185-187} Serum-alkaline phosphatase levels are also above normal in many cases in which osseous metastases are part of the clinical picture.¹⁸² Excessive acid phosphatase can be demonstrated by histologic examination of neoplastic prostatic tissue.¹⁸⁸ Dean, Woodard and Twombly¹⁸⁹ state that patients may be placed in four groups, based on the serum-phosphatase levels:

Normal men in whom there is no increase in either the serum acid or alkaline phosphatases. It is noteworthy that since every adult prostate contains large quantities of acid phosphatase and that the serum acid phosphatase of men is the same as that of women, who have no organ rich in acid phosphatase, this substance is prevented from entering the circulation by an intact prostatic capsule.

Patients with cancers of the prostate and normal amounts of serum acid and alkaline phosphatase. In this small but definite group one may operate with an excellent chance of removing all of the disease because the tumor probably has not grown beyond the gland.

A group consisting of the great majority of patients with prostatic carcinoma. The tumor has grown through the gland capsule and there may or may not be distant metastases. In our experience 73 per cent of these patients show increased serum acid phosphatase.

Patients with prostatic cancers which metastasize to bones. There is nearly always an increase in the serum alkaline phosphatase in these cases. The quantity of this substance in the serum so accurately represents the amount of reaction of the bones to the invasion of prostatic carcinoma that quantitative assays give clinical information not obtained by any other tests, such as the roentgen rays.

Castration and injection of estrogens produce little change in the acid phosphatase level if it is normal before such therapy.¹⁸⁹ Castration and injection of estrogens, however, into patients with prostatic cancer having marked elevation of the acid phosphatase result in a sharp reduction of the levels of the enzyme, but seldom to normal.¹⁹⁰ Administration of androgens produces a sharp rise in the serum acid phosphatase.¹⁹⁰ Alkaline phosphatase following castration or injection of estrogens into patients with metastatic disease may rise, show no change or decrease, either at once or after a latent period.¹⁸⁹ These observations have been of inestimable value in the diagnosis of the extent and recurrence of the disease.

Castration or the administration of estrogens, or both, produce apparent regressions of the prostatic lesions and their metastases in many patients.^{188, 189, 191-193} Serial biopsies of the tumor reveal marked degenerative changes in the cells when stilbestrol is given over a fairly long period of time.¹⁹⁴ Administration of androgens seems to increase the activity of the process.^{190, 195}

Excretion studies of the sex hormones in the untreated case before and after castration or hormone administration are of interest. Following castration a decreased estrogen excretion has been reported, whereas the 17-ketosteroids (androgens) after a slight initial fall may rise above the pre-

treatment level.^{189, 195, 196} Pituitary gonadotropin increases in the urine following castration, as is the case in menopausal or castrated women or in men who have undergone the climacteric. Injection of estrogens may decrease the 17-ketosteroids and pituitary gonadotropic levels in the urine, and the urinary estrogen titers may rise.¹⁸⁹ Thus it appears that the mechanism by which these two methods produce their similar beneficial effect may be somewhat different. The primary effect in the case of estrogen therapy seems to be on the tropic functions of the anterior pituitary gland, which are inhibited and in turn result in decreased stimulation of the organs that may produce androgens (gonads and adrenal glands). Castration, although removing one source of androgens, allows for increased pituitary activity, which may stimulate other organs, such as the adrenal glands, to increased androgen production.

Concerning the therapeutic value and marked clinical improvement following castration or estrogen administration, or both, there can be no doubt. It is still unsettled which form of therapy is the best. Castration or estrogens alone or in combination either simultaneously or successively all have their adherents. The greatest hopes for the treatment, however, have not materialized. Certain cases do not respond to treatment at all, whereas others show striking clinical improvement and relief from pain. This may be related to the histologic type of tumor, since those lesions that more nearly resemble the adult gland seem to respond best to the therapy.¹⁹³ It has also been conceded that the treatment in itself cannot be considered a curative procedure but should be reserved for palliative purposes. To date, there is no substitute for radical surgical procedures in operable cancer of the prostate without metastases. On the basis of present evidence, castration or hormone therapy should not be resorted to as the primary treatment in this type of case. Most patients who benefit from castration or estrogen therapy have recurrence of the signs and symptoms within a few years and many are not relieved for more than a few months.^{189, 193, 197} Some patients live without symptoms or obvious signs of activity of the disease for long periods of time, but as yet there is no definite evidence of true curability. It must be remembered that cancer of the prostate varies in its course and degree of malignancy so that the untreated patient or those receiving palliative surgical measures may live for a long time without benefit of any other form of therapy.¹⁵⁵ The final answer must await longer periods of observation.

Tumors of Testis

Tumors of the testicle are essentially diseases of the young. Approximately 75 per cent of the lesions arise in patients under the age of forty, and the average age incidence is about thirty-five.^{155, 198}

out that cancer of the endometrium is oftener associated with cancer of the breast and fibromyomas of the uterus than is cancer of the cervix.^{156, 164, 165} Hormone-excretion studies of significance in this disease have not been reported.

Fibromyomas. Many believe that fibromyomas of the uterus result from ovarian dysfunction. This is based particularly on the association of follicle cysts and endometrial hyperplasia with the disease, thereby suggesting excessive estrogenic stimulation,¹⁶⁶ but weighty evidence suggests that this is not the case. For example, Meyer¹⁶⁷ stressed that patients with fibroids become pregnant, menstruate normally and undergo typical cyclic changes, all of which is against ovarian dysfunction as a cause of the disease. It is well known that a certain number of lesions regress after the menopause or castration. This is far from constant and, as has been pointed out, may be related to the blood supply, especially since fibroids with adhesions to extrapelvic organs may continue to grow.¹⁶⁶ There are reports on the regression of fibroid tumors after treatment with testosterone and progesterone, but these are difficult to assess. A study of the excretion rates of the sex hormones in this disease failed to reveal any gross abnormalities.¹⁶⁸ Thus far the only convincing evidence for a hormonal etiology is the regression of the tumors after ovarian activity has ceased.

Tumors of Prostate Gland

Hypertrophy of prostate gland. Benign prostatic hypertrophy, that is, nodular hyperplasia, occurs in men over forty years of age. The disease increases with advancing age, so that between the ages of eighty and ninety, 75 per cent of men have some degree of nodular hyperplasia.¹⁰⁸ Obstructive symptoms, however, reach a maximum at about sixty-three years. As suggested by Moore,¹⁰⁸ this may mean that the etiologic agent becomes active after forty years of age, reaches its maximum soon after sixty and then decreases in intensity, but still remains capable of producing additional or new nodules. Some statistics indicate that benign hypertrophy is less frequent in single men.¹⁶⁹ Nodular hyperplasia of the prostate does not occur in the posterior lobe. Moszkowicz¹⁷⁰ showed that the structure of the prostate in the pseudohermaphrodite is dependent on the type of gonad present: the prostate is composed only of the middle and lateral lobes in the presence of ovaries, whereas in the presence of testes the entire prostate is found. These observations indicate that the posterior lobe is primarily a masculine organ, whereas the other lobes are ambisexual, that is, they can be stimulated by both estrogens and androgens.¹⁰⁸ There is no direct relation between the histologic appearance of the testes and benign prostatic hypertrophy. A survey of the literature by Moore¹⁰⁸ revealed, however, that, in a series of 28 eunuchs, eunuchoids

and those with pituitary infantilism in whom the secondary sex characteristics were lost before the age of forty, there was not a single case of the disease, even though they all lived to be over forty-five years of age. The incidence would be quite high in a similar age group in the normal population. Hence, it appears that the disease does not develop in the absence of the testes.

The changes in the prostates of patients with testicular tumors are not consistent. Cases occur in children in whom signs of adrenal insufficiency are accompanied by those associated with adrenal hyperfunction, particularly the masculinizing syndrome. In these children there is a hyperplasia of the prostate gland similar to what occurs in adults with functioning adrenocortical tumors.¹⁷¹ In primary Addison's disease the prostate does not differ from that in normal subjects.¹⁰⁸ Estrogens and androgens have been used in the treatment of benign prostatic hypertrophy, and although beneficial effects are said to occur, the consensus at present is that they are infrequently of any value.¹⁷² Castration has also been reported as beneficial, but this too is controversial.¹⁷³ Excretion studies of the sex hormones suggest a decrease in androgens and estrogens in those patients as contrasted with the levels in normal men of the same age.^{174, 175} Thus these observations, although not conclusive, suggest an endocrine dysfunction as a possible etiologic factor in the disease.

Cancer of prostate. The median age at the onset in 235 cases with cancer of the prostate was sixty-five.¹⁵⁵ It is rare below the age of thirty and increases steadily with advancing age. In fact in the eighth decade of life it is one of the most frequent of all carcinomas.¹⁷⁶ Prostatic cancer is rare in the Chinese¹⁷⁷ and has not been recorded in eunuchs or eunuchoids.¹⁰⁸ Routine autopsy studies of the prostate in man reveal an incidence of 10 to 15 per cent of latent carcinoma.¹⁷⁸⁻¹⁸⁰ On one series of unselected consecutive autopsies on 50 men over fifty years of age, however, the prostate was examined by serial section and the incidence of occult carcinoma was 46 per cent, although prostatic carcinoma was not the cause of death in any case.¹⁸⁰

Following the progress report of Quinby¹⁸¹ in 1942 more material has accumulated, and it may be of interest to bring this up to date. Although castration was previously suggested and occasionally used as a treatment for cancer of the prostate, it was not until the excellent work of Huggins and his group^{109, 110} on the effect of the hormones on the prostate and that of the Gutmans¹⁸² on acid phosphatase that investigation of the hormonal relation to the disease received a real stimulus. The prostate in childhood contains small amounts of acid phosphatase, but the level rises considerably after puberty.¹⁸³ This enzyme, which is present apparently in large amounts only in the prostate,

hormone excretion is of the greatest value in patients who have functioning tumors of the adrenal glands and the gonads, such as adrenocortical hyperplasias, adenomas and carcinomas, granulosa-theca-cell tumors of the ovary, arrhenotomas, and teratoid tumors and interstitial-cell tumors of the testes. The excretion rates in these cases are of inestimable help in making the diagnosis and in following the course of the disease. Recent studies on the isolation of the sex hormones suggest that patients with cancer may excrete estrogens and 17-ketosteroids in a different fashion from persons without cancer. The usual relation of the individual components of both the estrogens²⁰⁸ and 17-ketosteroids^{209, 210} may be atypical as well as the ratio between the total estrogenic and 17-ketosteroid complexes. It is clear that alterations in excretion levels or in the specific type of hormone excreted are not necessarily characteristic of patients with cancer. They may merely represent deviations from normal that occur only as a result of disturbed metabolism in the sick person. They indicate, however, a distinct abnormality, and as such are significant in the study of the disease.

CONCLUSIONS

A considerable number of data bearing on the relation of the endocrine organs to tumors have accumulated. The administration of sex hormones to experimental animals has resulted in the production, the augmentation and the inhibition of benign and malignant tumors. These changes are limited to definite types of tumors in different species, as well as to certain strains in any one species of animal. Thus, there are other factors that determine the reaction of a tumor to a hormonal stimulus, and the susceptibility of an animal to the induction of a neoplasm. It is difficult to interpret these facts in terms of human cancer. Nevertheless, they are of extreme importance in the study of the origin and course of cancer in general.

Strong evidence exists to indicate that endocrine factors are associated with some human tumors. There is as yet no conclusive proof that these influences are directly concerned with cancer, although an increasing number of cases are coming to light in which cancer developed after intensive estrogen therapy in organs such as the uterus and breast, which are normally stimulated by these hormones. It is probable that this is coincidence, but the association cannot be ignored. Present evidence suggests that the sex hormones are not in themselves carcinogenic. It is likelier that, as a result of excessive stimulation or atypical metabolism, the tissues of susceptible persons are conditioned to the action of a carcinogenic agent.

There is little to support the therapeutic value of hormones in the treatment of any cancer except that of prostatic origin. Judgment must be re-

served until much more information is obtained regarding the treatment of cancer of the breast or other organs with either estrogens or androgens. There is no question that castration as an adjunct to the treatment of selected cases of cancer of the breast and prostate and the administration of estrogens to patients with cancer of the prostate have been of great benefit. Such treatment should be reserved for palliative purposes only, since there is at present no substitute for established methods of surgery and radiation in the operable patient. Indiscriminate use of the sex hormones may also produce untoward effects in other ways. It therefore behooves all to be extremely cautious in the use of the sex hormones for any syndrome, even when the indication for treatment is well defined.

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In other words, these tumors appear at a time when the male is most active sexually. This age incidence is distinctly different from that of most other types of malignant neoplasm and suggests causation by other agents. It is also well recognized that tumors of the testicle occur more frequently in men with undescended testes. Gilbert and Hamilton¹⁹⁹ found that in 345 of 835 reported cases of teratoma of the testicle the lesions were intra-abdominal. Eleven per cent of the 345 occurred in pseudohermaphrodites. This does not mean that when unilateral cryptorchidism is present the tumors always appear in the undescended testis. In one study it was found that the tumor occurred in the normal gonad in 23 of 744 patients with unilateral cryptorchidism,¹⁹⁹ and in another series the incidence was 6 in 27 cases.¹⁹⁸ These findings, however, suggest a possible hormonal factor.

Excretion studies of the hormones are of great interest in tumors of the testicle. Gonadotropic substances are often excreted in increased amounts in the urine of patients with testicular tumors.²⁰⁰ Two types have been identified — one similar to the chorionic gonadotropin normally found in the urine of pregnant women,²⁰¹ and the other a gonadotropin similar to that found in human beings who have been castrated or who have passed through the menopause.²⁰² The latter will be referred to as the pituitary type of gonadotropin. Some malignant tumors of the testes, although histologically similar to those resulting in increased secretion of gonadotropins, fail to show any increase; clinically such cases behave identically with those in which the hormone titer is elevated.^{198,202} Furthermore, as pointed out by Hamburger²⁰² and by Twombly,¹⁹⁸ the pituitary type of gonadotropin may be present in increased quantities in the urine in the absence of active tumors. It does not vary with treatment or progression of the disease. Although it was formerly thought that the amount of hormone excreted paralleled the degree of malignancy of the tumor, it has recently been shown that this cannot be relied on to be pathognomonic of cell type, any more than can the nature of the hormone excreted.²⁰³ In general, however, chorionic gonadotropin is likelier to be associated with embryonal adenocarcinomas and chorioepitheliomas, whereas elevations of the pituitary type of hormone usually accompany seminomas, there being exceptions in both groups. Both hormones are often found in the same patient, which suggests that many testicular tumors consist of mixed cell types.^{198, 204, 205}

These hormone studies are of interest in prognosis. It has been stated that cases showing unusually large amounts of the hormones in the urine have a poor prognosis. Hamburger, Bang, and Nielsen²⁰¹ based their observations, however, on differentiation of the two forms of hormones excreted. They are of the opinion that the chorionic type is secreted by the tumor, since this hormone is biologically similar

to that secreted by the normal placenta. Moreover, there appears to be a close correlation between the amount excreted and the extent of the neoplastic disease. Twombly¹⁹⁸ states that this type of hormone in male urine does not appear except when tumor is proved to be present. Several observers agree that the chorionic gonadotropin is likely to be indicative of a radioresistant type of tumor, whereas tumors associated with an increased excretion of the pituitary type of gonadotropin are usually radiosensitive.²⁰⁴ Excretion studies are also of value in studying the course of the disease. If there are no metastases and the tumor is secreting large amounts of hormones, orchidectomy will usually be followed by a prompt disappearance of the hormones. If metastases appear subsequently, the hormone levels may again rise, and in some cases may predict recurrences before they can be detected clinically. If metastases are present at the time of orchidectomy the titer may show little change. The effectiveness of x-ray therapy in the metastatic lesions in some cases may also be determined by a study of the excretion rates.

Abnormal estrogen excretion may be found in the presence of these tumors, particularly those that produce large amounts of chorionic gonadotropin.¹⁹⁹ Pregnandiol, the excretion product of the corpus luteum hormone, was also found to be elevated in one case of chorioepithelioma.¹⁹⁸

The excretion of biologically active androgens is definitely decreased in a high percentage of seminomas.²⁰⁶ In cases showing chorionic gonadotropin, levels below normal were found in about half the cases studied. Hamburger and Godtfredsen²⁰⁶ believe that the formation of chorionic gonadotropin may stimulate the remaining testis and the adrenal glands, causing the production of male hormone. This might explain the difference in the findings between these two types of tumors.

Attempts to influence the course of testicular tumors by hormones have been made by Twombly.¹⁹⁸ Administration of antigonadotropic principles resulted in the increase of the hormone titers. Estrogens were also tried on 2 patients without any striking change. Saleeby²⁰⁷ suggested that bilateral gonadectomy should be done and cites a case in which the patient seemed to improve after the procedure was carried out. Evaluation is complicated, however, by the fact that the patient had x-ray therapy as well.

SIGNIFICANCE OF HORMONE EXCRETION

Urinary excretion levels of the sex hormones represent only the end product of metabolism. It is not definitely known whether they give true indices of the blood levels, the rate of secretion or destruction and the utilization of the hormones by the tissues. Furthermore, they do not reveal the exact nature or relation of the various components of the hormones excreted. Thus far, the study of

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 30501

PRESENTATION OF CASE

First admission. A forty-nine-year-old electrician was admitted to the hospital with substernal pain of twenty-four hours' duration.

The patient was well until the day before admission, when he suddenly developed a sensation of breathlessness and a lump in his throat. This

mission the pain appeared to be epigastric, radiating to the top of the sternum. For five years prior to admission the patient had had attacks of "indigestion" associated with pain radiating to the head and with spots before the eyes.

Physical examination revealed a well-developed and well-nourished, restless man complaining of substernal pain. The skin was dry, and the heart, lungs and abdomen were normal.

The temperature was 100°F., the pulse 68, and the respirations 16. The blood pressure was 140 systolic, 90 diastolic.

Examination of the blood showed a red-cell count of 5,000,000, with 17.5 gm. of hemoglobin, and a white-cell count of 15,000, with 80 per cent neutrophils. The urine and stools were normal. The erythrocytic sedimentation rate was 24 mm. per hour, total fall (0.8 mm. per minute, corrected). The serum cholesterol was 292 mg. per 100 cc.

An electrocardiogram taken on admission re-

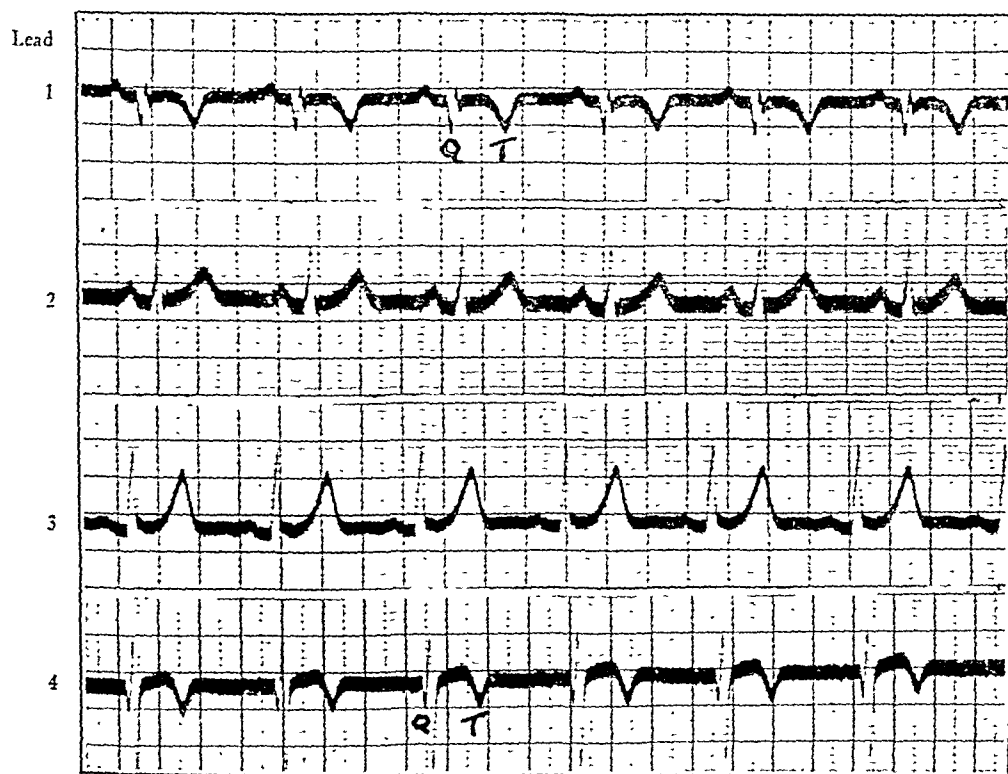


FIGURE 1. Electrocardiogram during the Acute Anterior Myocardial Infarction in 1942.

lasted a few moments and was followed an hour later by a squeezing sensation beneath the sternum, with pain radiating to the deltoid region and down the extensor surface of the right arm. This was accompanied by nausea and a recurrence of the feeling of breathlessness. A physician gave him "an injection and some pills." He vomited eight times during the night. On the morning of ad-

mission the pain appeared to be epigastric, radiating to the top of the sternum. For five years prior to admission the patient had had attacks of "indigestion" associated with pain radiating to the head and with spots before the eyes.

The patient was treated with morphine and bed rest and quickly became asymptomatic. The temperature fell to normal on the fifth hospital day, and the white-cell count gradually fell to 7600 over a period of about two weeks. The corrected sedimentation rate gradually fell to 0.6 mm. per minute. A subsequent electrocardiogram (Fig. 1) showed

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labored respirations. The heart sounds were distant and a Grade 2 blowing systolic murmur was present at the apex. There was slight dullness on the right side of the chest, with increase in the

The temperature was 100.4°F., the pulse 96, and the respirations 30. The blood pressure was 110 systolic, 75 diastolic.

Examination of the blood showed a white-cell

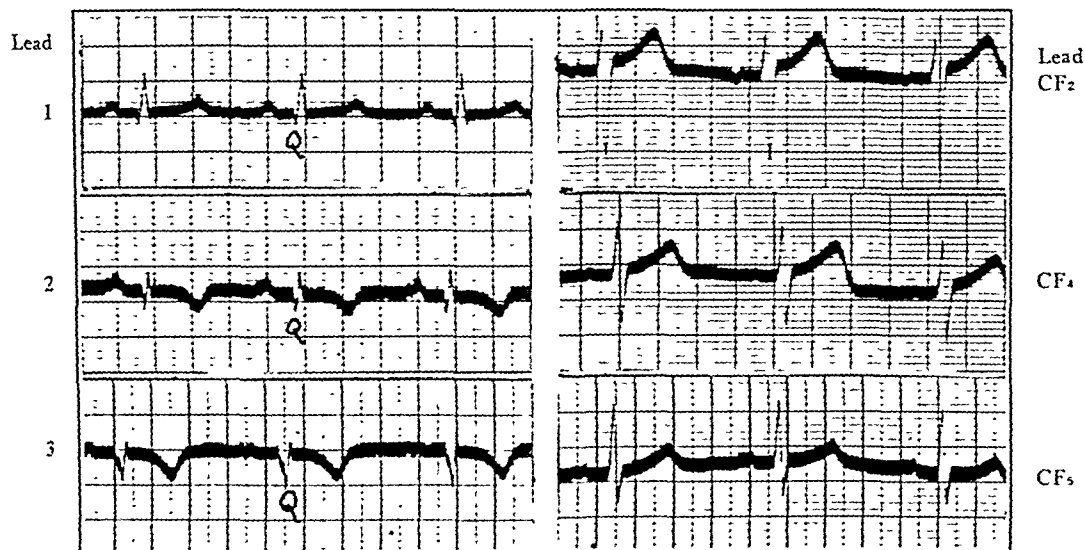


FIGURE 3. *Electrocardiogram Taken Three Weeks after That in Figure 2 and Showing Normal Precordial Leads.*

whispered voice. Numerous medium moist rales were present at both lung bases and at the right

count of 23,700, with 92 per cent neutrophils. The serum nonprotein nitrogen was 57 mg. per 100 cc.,

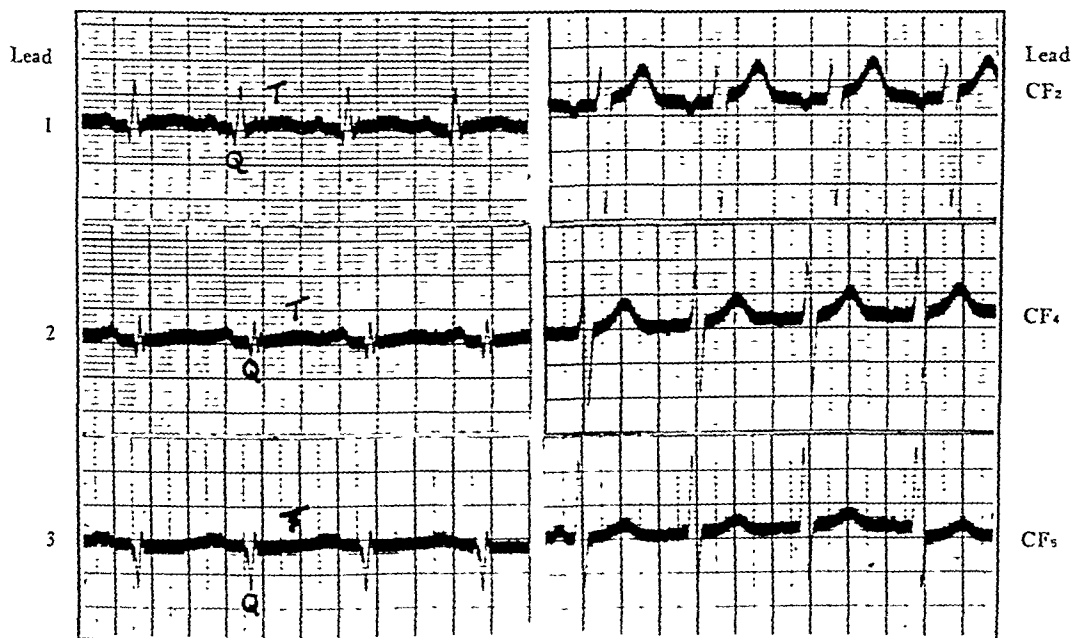


FIGURE 4. *Electrocardiogram Taken Slightly More Than Two Months after the Posterior Myocardial Infarction.*

apex posteriorly. There was slight tenderness in the left lower quadrant of the abdomen. The knee jerks were hypoactive, and the Babinski positive bilaterally.

and the protein 6.7 gm.; the chloride was 94 milliequiv. per liter.

On the evening of admission the patient coughed up thick orange-colored sputum for the first time.

changes characteristic of involution of a large anterior-wall infarction with prominent Q waves and inverted T waves in Leads 1 and 4. He was discharged on the forty-second hospital day.

Second admission (eight months later). Following discharge the patient was followed in the Out-Patient Department, where he showed progressive improvement. He continued to have slight precordial pain, however, with mild choking sensations and dyspnea.

Two nights before his second admission, after a day of unusual exertion, he suddenly developed severe substernal pain radiating down both arms

version of the T waves in Leads 1 and CF₄. A subsequent tracing (Fig. 3) showed a return to normal rhythm, and the remaining changes were considered characteristic of the evolution of a posterior-wall infarction. The temperature and white-cell count rapidly returned to normal. He was discharged on the thirty-fifth hospital day.

Final admission (one year later). Following discharge the patient was unable to work and remained at home. An electrocardiogram two months after discharge (Fig. 4) showed normal rhythm at a rate of 100, with small Q waves and low T waves in Leads 1, 2 and 3 and fairly normal tracings in

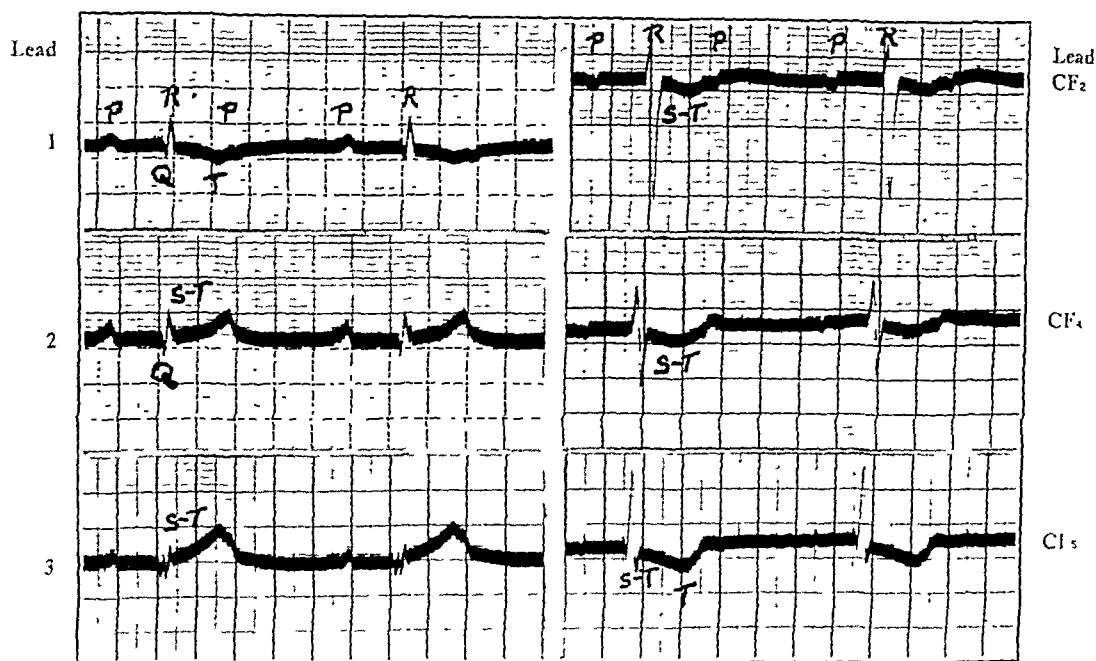


FIGURE 2. Electrocardiogram during the Acute Posterior Myocardial Infarction in 1943.

and relieved by nitroglycerin. He spent a restless night in moderate discomfort and remained in bed the following day. On the evening before admission a similar but severer attack occurred, which was accompanied by a sense of suffocation.

On admission the physical examination was negative except for an inconstant gallop rhythm at the apex, thought to be systolic. The white-cell count was 19,600, with 89 per cent neutrophils.

On admission, the temperature was 96.4°F., rapidly rising to 102°, the pulse 54, rising to 100, and the respirations 20. The blood pressure was 160 systolic, 100 diastolic.

An electrocardiogram (Fig. 2) showed 2:1 auriculo-ventricular block, with a ventricular rate (R) of 50 and an auricular rate (P) of 100. Q₁ and Q₂ were small. There was depression of the ST segments in the precordial leads (CF₂, CF₄ and CF₅), with elevation in Leads 2 and 3. There was late in-

version of the T waves in Leads 1 and CF₄; it was much more normal in appearance than the previous records (Figs. 1, 2 and 3). He had, however, frequent attacks of pain in the right wrist radiating up the arm and across the upper chest, usually precipitated by slight exertion but occasionally occurring while at rest; these were relieved by nitroglycerin. On the day before admission he had such an attack; it was extremely severe and was relieved by nitroglycerin only for brief periods. Several hypodermic injections gave no relief. He also noted a dull pain over the lower right chest anteriorly. He felt weak and was dyspneic. During the night the pain in the arms and chest continued. He developed a dry hacking cough, was nauseated and perspired freely. He was admitted to the hospital the following morning.

Physical examination revealed an acutely ill, cyanotic man with warm, moist skin and rapid.

The onset of pain on the final admission seemed to be similar in nature to the pain that he had had during the year previous to entry. It makes one think seriously of the possibility of his having had a third myocardial infarction. We might follow that line of reasoning and say that with this attack he went into congestive failure, that he developed edema of the lungs and diminished urinary output, with nitrogen retention, and that he had cerebral anoxia. That might have accounted for the positive Babinski and the increasing disorientation. We might go farther and say that he developed bronchopneumonia, which was responsible for the fever.

I think we ought to review the findings at the time of the last admission to see if there is anything against that diagnosis. The first thing is the dull pain over the right lower chest anteriorly. I do not consider this as being typical of the pain of myocardial infarction. I did consider the possibility of small pulmonary infarcts. In the examination of the heart I was surprised that he did not have gallop rhythm. This might have been present but not detected. I cannot explain tenderness in the left lower quadrant of the abdomen on the basis of recent myocardial infarction, and I do not know whether it is significant. I should think that the positive Babinski in a fifty-year-old man, even if he did have considerable anoxemia, is a rather unusual finding, and possibly one ought to consider some other lesion of the brain. The rise in the non-protein nitrogen can reasonably be explained on the basis of the fall in blood pressure and a certain amount of nephrosclerosis. Concerning the culture of the sputum, I do not know whether the few beta-hemolytic streptococci have any significance. It must be considered, however, in the face of the high temperature. Curiously, the first chest film showed a normal-sized heart and a few days later another film showed an enlarged heart.

Perhaps this would be a good time to look at the films.

DR. MAURICE FREMONT-SMITH: How far apart were the examinations?

DR. LAURENCE L. ROBBINS: Four days; but the last film was so poor that I did not put it up. The heart is probably enlarged in this film, but the film was taken anteroposteriorly instead of postero-anteriorly, and I am not impressed with the size of the heart. There is increased density in both upper lung fields and in the middle portions of the lower lung fields. These areas are clearer on the last film, but I still think that there is some increase in density; it is not particularly well defined, but there are mottled areas scattered throughout.

DR. HARWOOD: Are they characteristic of any lesion?

DR. ROBBINS: They could be pulmonary infarcts but they certainly are not typical; they could be caused by congestion.

DR. HARWOOD: The electrocardiogram showed little change considering the pain. I do not set

myself up to be an expert on this type of examination, but I believe that this patient had marked changes in the ST segment in the T waves in both of the previous attacks. If this were a fresh infarction, I should expect to see more than an inverted T₁ after six days. Will you comment on that, Dr. White?

DR. PAUL D. WHITE: On the first admission in 1942 the record was absolutely characteristic of anterior myocardial infarction in both the limb leads and the precordial leads (Fig. 1). On the second admission, in 1943, a year before the patient died, he had absolutely typical evidence of posterior myocardial infarction superimposed on the changes due to the anterior scar (Fig. 2). It is interesting that he had heart block the second time; this is more frequently found after posterior myocardial infarction with thrombosis of either the left or the right circumflex vessel. The heart block cleared up entirely, as it usually does (Fig. 3). During his convalescence from the second myocardial infarct the electrocardiographic leads looked much better than after the first infarct. A neutralization of the "bad" features of the electrocardiogram that resulted from the first attack was effected by the second attack, even though there was actually more heart disease, for the reason that the T waves became upright again in both Lead I and in the precordial leads, as is shown in Figure 4, an electrocardiogram taken two months after the second attack. After posterior infarction the record never looks so "bad" as after anterior infarction, since inversion of T₁ may occur normally and does not appear so abnormal as inversion of T₁. The neutralization effect of the two lesions, front and back, was more or less maintained at the time of the last admission, and it becomes rather difficult to say from the electrocardiogram (Fig. 5) what happened at that time. Clinical evidence becomes all the more important because of this very difficulty. The limb leads show lower voltage without any especially acute changes in the T waves or ST segments but there is some change in the QRS waves, especially in Leads 2, 3, CF₄ and CF₁, and there is a simple tachycardia superimposed. The combination of lesions that had occurred before might explain the majority of the abnormalities in these last electrocardiograms. There were still fairly good precordial leads, except for the QRS waves in Leads CF₄ and CF₁ on the final admission, and the T waves and ST segments were better than those at the time of the other two admissions. One great difficulty is that, when one has coronary heart disease, anything that disturbs the circulation functionally can also cause changes in the electrocardiogram that are not necessarily due to structural damage.

DR. HARWOOD: It seems to me that we have to decide whether this patient had a fresh infarction, with resulting congestive failure, and terminal bronchopneumonia, or whether he had some other event, such as infection or pulmonary infarction,

culture of which revealed a few beta-hemolytic streptococci. A roentgenogram of the chest revealed increased density in both upper lobes and in the medial portions of both lower lobes; this showed some clearing four days later. The heart appeared normal. An electrocardiogram (Fig. 5) showed sinus tachycardia of 120, with low T waves in all leads. The QRS waves in Leads 1, 2 and 3 were low in voltage. This was not significantly different from a tracing taken nine months before, but wide Q waves had appeared in Leads CF_4 and CF_5 . Six days later T_3 was slightly inverted.

The patient was treated with tourniquets, oxygen, morphine and Cedilanid, with some initial improve-

ment. The temperature continued to rise, however, eventually reaching $104.8^{\circ}F.$, with a pulse of 140 and respirations of 50. The serum nonprotein nitrogen rose to 110 mg. per 100 cc. The lung signs cleared considerably, but the patient became increasingly disoriented. An x-ray examination of the chest at that time revealed an enlarged heart with a rather diffuse haziness over both lung fields suggestive of pulmonary edema but with no frank area of pneumonia. His respirations became acidotic, and he died on the seventh hospital day.

Then we come to the final admission one year later. I should like to ask about the acidotic respirations. Since the man had rapid labored breathing on admission and some evidence of congestive failure, I should like to know how one can differentiate the type of breathing.

DR. ROBERT L. BERG: I saw the patient, and I believe that he had not only rapid and shallow respirations but also a uremic odor to his breath.

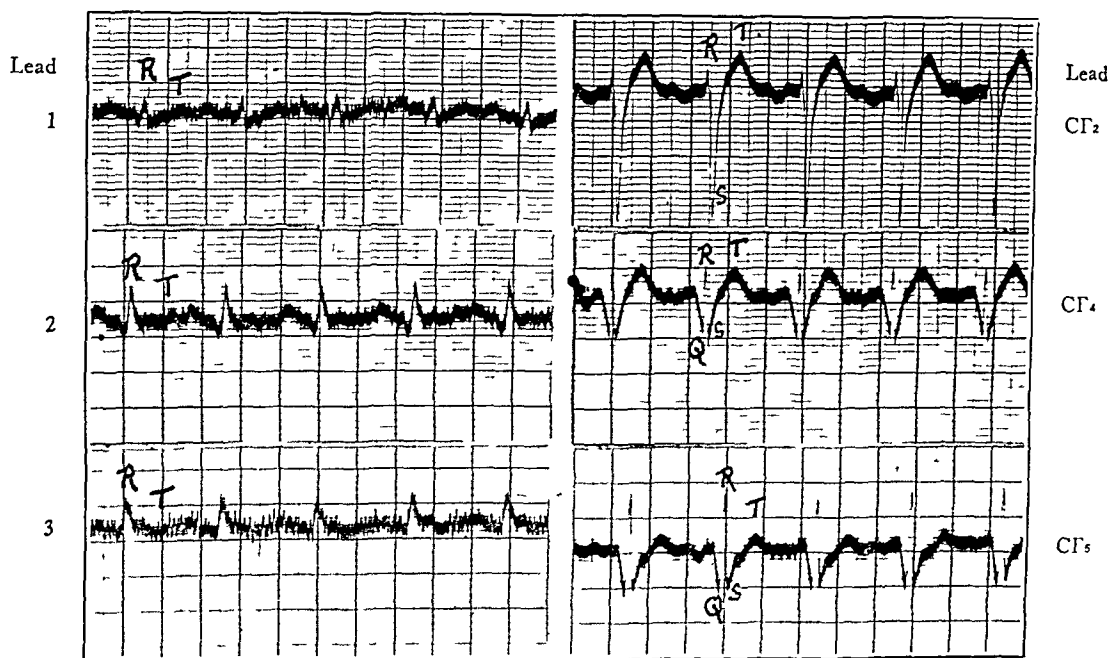


FIGURE 5. Electrocardiogram Taken in 1944, the Year after the Second Attack and One Day after the Onset of the Final Illness.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD: The first two admissions in this case can be summarized briefly. At the age of forty-nine, twenty months before death, this patient came into the hospital with a history, physical examination and electrocardiographic findings typical of a large anterior myocardial infarction. On the second admission, eight months later, the patient

had a similar episode, the electrocardiograms being classic for posterior myocardial infarction. The only other thing worth mentioning in the initial admission is that he had a serum cholesterol of 292 mg., which is rather high.

DR. HARWOOD: Then we have to qualify that statement. It might have been actual dyspnea, with a uremic odor to the breath.

I am also interested in the urinalyses. The only one reported was done at the time of the first admission, and that was negative.

DR. BENJAMIN CASTLEMAN: The urinary sediment showed 2 to 12 white cells and an occasional epithelial cell per high-power field. There was no albumin or sugar. On admission he had a +++ test for acetone, but that disappeared. The specific gravity was 1.034 on admission, and 1.020 and 1.024 after that.

DR. HARWOOD: May I ask about the urinary output during his final stay in the hospital?

DR. CASTLEMAN: You may look at the chart.

DR. HARWOOD: The output was 500 cc. in the first twenty-four hours, and rose to 1500 cc. on the fourth day; it was 1250 cc. on the next day, and fell off to 300 cc. on the last day.

DR. WHITE: Human electrocardiography began with chest leads; the first record ever published, and probably taken, was by Waller¹ in 1887, who placed one electrode on the front of the chest and one on the back. The capillary electrometer then used was exceedingly clumsy, and it was not until the string galvanometer was introduced in 1903 by Einthoven² that clinical electrocardiography became feasible.

In those early years it was the custom to take the limb leads, for convenience largely, but when certain electrocardiographers like Lewis³ wanted to explore the thorax to get better records of auricular action, they did put electrodes over the heart, chiefly over the sternum in the region of the right auricle. In the course of time a number of investigators explored the chest, including Dr. Burwell and myself,⁴ in the search for other planes than the frontal for determination of the projection of the electrical axis. Dr. Burwell and I wanted to study, for example, the electrical axis in space to get more idea of the size of the left ventricle. This did not pan out at the time because we did not appreciate the importance of the proximity of one of the electrodes to the heart itself.

As time went on, Wilson⁵ in Ann Arbor and Wood⁶ and Wolferth⁷ in Philadelphia studied leads taken with electrodes placed on the chest directly over the heart. It has been found that direct leads from the heart itself show best the condition of the underlying myocardium and that next best are the leads taken from the chest wall as near as possible to the heart. Thus some ten or twelve years ago precordial electrocardiography began.

In the early days of clinical precordial electrocardiography its application was rather hit or miss; often just one electrode was applied and that, as a rule, was placed at the apex of the heart; in fact, this apical lead, with the other electrode placed on one of the extremities, became the recently current, and still customary, Lead 4. This apical lead has often been extremely helpful, being abnormal in some cases, especially those of coronary heart disease, in which the usual limb leads (Leads 1, 2 and 3) are normal, but such a finding is dependent on the proximity of the cardiac damage to the exploring electrode, whereas lesions elsewhere or abnormalities of the heart chambers other than that of the ventricle directly underlying the electrode are likely to be missed when only one single precordial lead (Lead 4) is taken.

During the last ten years a great deal of study has been carried out using multiple precordial leads, but much of this is still in the investigative stage. Precordial leads, however, have been numbered so that physicians will know about what the cardiologists are talking. The first precordial lead point is just at the right of the sternum in the fourth intercostal space. The second precordial lead point is just to the left of the sternum in the fourth inter-

costal space. The third precordial lead point is midway between the second and fourth on a direct line, the fourth being not necessarily the same as the routine Lead 4 but placed in the midclavicular line, usually in the fifth interspace on a line between the second precordial lead point and the cardiac apex. The fifth precordial lead point is on a horizontal line from the fourth in the anterior axillary line, and the sixth is in the midaxillary line. Other lead points have been suggested, such as a seventh in the posterior axillary line or at the angle of the left scapula and so forth, but we recognize officially only these six leads at the present time. The indifferent electrode, that is, the other electrode, can be placed either on the right arm (when we speak of the precordial leads as CR₁₋₆), on the left arm (when we speak of the precordial leads as CL₁₋₆), on the left leg (when we speak of the precordial leads as CF₁₋₆), or on a junction point of the three, Wilson's lead, in which the effect of any one extremity is neutralized by the others (when we speak of the precordial leads as CV₁₋₆). Thus, actually twenty-four precordial leads may be taken.

We have made a special study of about 175 cases, normal and abnormal, using these twenty-four precordial leads and have learned a good deal, but of course, they are not applied routinely. In fact, a good many cases need no precordial leads. In doubtful cases, especially those in which coronary insufficiency or massive pulmonary embolism is suspected, in cases of hypertension and coronary heart disease and for complete examination, precordial electrocardiography is in order.

Finally, we come to the practical application of these various precordial leads to clinical electrocardiography. Two reports have been published by the American Heart Association through its Committee for Standardization of Precordial Leads,^{8,9} but neither of them is final because there has been no exact agreement concerning which precordial leads are to be advised. It is the consensus among experienced electrocardiographers that more than one precordial lead is important in order to see what is going on over the right ventricle, as well as over different parts of the left ventricle and the septum. In the last report of the American Heart Association three precordial leads were advised, namely, C₁, C₂ and C₃. We, however, and a number of others, have found that it is more practical and of greater value to use C₂, C₄ and C₆, which, as a rule, are located as follows: C₂ over the right ventricle, C₄ at the junction of the right and left ventricle, and C₆ over the left ventricle. It is astonishing how much difference there often is between C₄ and C₆ if C₄ is over the right ventricle and C₆ is over the left, or if one of these leads has a lesion directly underneath it. For the indifferent lead point we prefer the left leg. One is likelier to find abnormalities with that connection than with the others, although there are

that by increasing the strain on the heart produced both coronary and myocardial failure. I am inclined to favor the latter, on the basis of the rather unusually high temperature and the rather minor signs or change in the electrocardiographic tracings.

Before closing I should like to mention two other possibilities that seem rather unlikely. One is a dissecting aneurysm, in which one would expect the blood pressure to stay much higher and the pain to be much worse. One would also expect to find evidence of circulatory changes in the extremities. I am going to exclude it. An extremely rare possibility is rupture of the heart through an aneurysm resulting from an old scar in the posterior part of the heart.* Ordinarily that produces sudden death, but I understand that occasionally there can be a slow leak. I simply mention it as a possibility, and I do not see how one can rule it in or out.

I also mention the possibility that mural thrombi were thrown off to the cerebral hemispheres and possibly to the mesentery, which would explain the positive Babinski, the increasing disorientation and the tenderness in the left lower quadrant of the abdomen.

DR. WHITE: It is quite possible that this final illness started with myocardial infarction. The symptomatology strongly suggests this, but I have never seen a death from myocardial infarction — and heart failure — with such a high temperature due to myocardial infarction alone. There was one change in the precordial leads† that I did not emphasize earlier, as I probably should have done,

*Later comment by Dr. White. I take issue with the statement by Dr. Harwood that the heart occasionally ruptures through an old scar. Rupture of the heart may occur through a fresh myocardial infarct, almost always within the first ten days or two weeks, but not through an old, healed and tough scar, even when there is a fairly well marked cardiac aneurysm of long standing. Two recent papers emphasize this point.^{10, 11} In a series of 270 cases of myocardial infarction found among nearly 3000 autopsies at the Massachusetts General Hospital from 1933 through 1940, there were included 165 cases of old infarction and 105 cases of fresh infarction. There were 10 cases of cardiac rupture in the whole series, but all were found among the cases with acute infarction. In the second paper, 47 cases of myocardial infarction were found in 115 consecutive autopsies carried out in patients in mental institutions in Massachusetts. Twenty-five of these cases showed old infarcts, and in none of these cases was there cardiac rupture, but among the 22 cases of recent infarction there were 16 with rupture of the heart. The difference between the incidences in the two series, which were 10 per cent and 73 per cent, respectively, was doubtless due to the fact that in the former there was as a rule, adequate rest therapy during the process of healing, whereas in the latter there was little or none at all.

†During the last few years it has become customary at the Massachusetts General Hospital to take multiple precordial leads in any important or doubtful case, instead of the limb leads alone or the limb leads and lead 4, which is the routine apical precordial lead. On rare occasions all six precordial leads, extending from C₁ (at the right of the sternum in the fourth interspace) to C₆ (the midaxillary line), are taken (see below). Generally, however, in the appropriate cases, as in the case cited here, the three routine precordial leads are taken that have been found to be the most helpful, namely, C₁ (with the electrode in the fourth interspace just to the left of the sternum), C₄ (with the electrode at the intersection of the midclavicular line and a line drawn from the C₂ point to the cardiac apex) and C₅ (in the anterior axillary line at the intersection of the horizontal line from the cardiac apex). These have been found, in the main, to be by far the most useful, and they are relatively simple to take. They demonstrate most of the changes underlying the lead points that concern the right ventricle and the anterior and lateral walls of the left ventricle. Lesions of the posterior wall of the left ventricle are not adequately shown by these lead points or by any others, except an esophageal lead.

In the case under discussion, Lead C₃ would probably have shown the greatest change, since it overlies the region of the septum. The letter C designates chest, and the letter F, which is added in the case discussion above, refers to foot and indicates that the left leg is the site of the indifferent lead point. If the right arm is used in the precordial leads, one speaks of CR, and if the left arm is used, one speaks of CL. On occasion Wilson's lead-point, off the body altogether but connecting all three extremities and called V, has been used as the indifferent point for the precordial leads. It (CV) gives the balance or average of the other three (CF, CR and CL).

and that, in prominent form, was seen in the electrocardiogram at the last admission (Fig. 5), namely deep Q waves in Leads CF₄ and CF₅. This may mean a new acute myocardial infarction, but my experience has not been sufficient in this particular for me to be absolutely sure of its presence or of its location.

CLINICAL DIAGNOSES

Coronary heart disease.
Cardiac failure.
Bronchopneumonia.

DR. HARWOOD'S DIAGNOSES

Coronary heart disease.
Cardiac failure.
Bronchopneumonia.
Pulmonary infarction?
Myocardial infarction, recent?

ANATOMICAL DIAGNOSES

Coronary thrombosis, old and recent.
Myocardial infarcts, old: left ventricle, anterior and posterior.
Myocardial infarct, recent, septal: left and right ventricles.
Mural thrombi, left and right ventricles.
Pulmonary infarcts.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed an enlarged heart, weighing 500 gm. There was an old anterior myocardial infarct, which was completely healed, and a posterior infarct, which was also healed. The coronary arteries showed old occlusions. There was, however, a recent occlusion in the descending branch of the left coronary artery, 2.5 cm. from its origin, as well as a large recent septal infarct involving both the left and the right ventricle, a most unusual occurrence. There were mural thrombi on both sides of the septum, those on the right apparently accounting for four large pulmonary infarcts in the right lower, right upper and left lower lobes. This is one of the few cases in which we can be fairly sure that the emboli arose from the right side of the heart, because careful examination of the leg veins revealed no thrombosis. Usually, even in the presence of mural thrombi in the right heart, we believe that such emboli come from the deep veins in the legs.

DR. WHITE: The chief clue in the electrocardiogram to the septal infarct was not in the limb leads but evidently comprised the deep Q waves in Leads CF₄ and CF₅; this finding was distinctly abnormal and had not been present before.

DR. CASTLEMAN: Because the current use of precordial leads in electrocardiography is not too well known, I have asked Dr. White to present a brief review of this subject.

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DECELERATION IN MEDICAL EDUCATION

SINCE September, 1941, the medical schools of the United States, by operating on a nine-month schedule, have done their best to meet the dire national need that became clear so suddenly after the attack at Pearl Harbor. The same motivation brought about a similar acceleration in the educational programs of our hospitals, where the 9-9-9 plan of rotating internships locked into the medical-school schedules, and of our colleges and even high schools, where premedical courses were given. There are now two indications that the pressure on this educational system may be reduced: the Army has altered its contract with the medical schools in such a way that, until further notice, it

will supply only 28 instead of 55 per cent of the matriculants, and the schools themselves are widely adopting the return to an annual period for the matriculation of future classes.

These moves on the part of the Army and of the medical schools call for rather prompt adjustments if future difficulties are to be avoided. They are not exactly movements in the same direction: the Army has reduced the number of its trainees but still calls for their continuous training and the medical schools have reduced the frequency of entering classes but are not yet in a position to return to a twelve-month basis. Unless the return to annual admission and a full-year course are made simultaneously and at the time — June — when courses formerly terminated, two things are bound to occur: first, for each year that the nine-month curriculum is retained, there will eventually be a delay of three months between medical-school graduations, with a maximum of a year, and second, when the twelve-month curriculum is resumed, the teaching schedules for three years will be chaotic. This brings up for immediate discussion, and for reasonably prompt decision, the question whether a return to the prewar timing of the curriculum is desirable.

This question has several phases. For the students at the top of the academic ladder, acceleration could be continued with profit and ease. These students can acquire in three years, as well as in four, the knowledge demanded, but there are not enough of them to supply the medical needs of the country — even in peacetime. The students at the bottom of the class in scholastic performance are definitely unable to complete the work satisfactorily in three calendar years, although many of them can do so in three and a half or four years. Many of these stable, hard-working students, who can do the work only if they are not hurried, have the attributes of character and personality that enhance their potential usefulness as physicians, and it is altogether proper that such persons be accorded some elasticity and consideration in the planning of the medical curriculum. The great majority of the students, however, stand in between these two ends of the academic ladder: they are the common denominators, they set the pace that the

occasions when a connection with the right arm or the left arm will be more useful. There is a scheme by which one can pick out the preferable lead, but it is complicated and for routine use during the past two years we have been using Leads CF_2 , CF_4 , and CF_6 .

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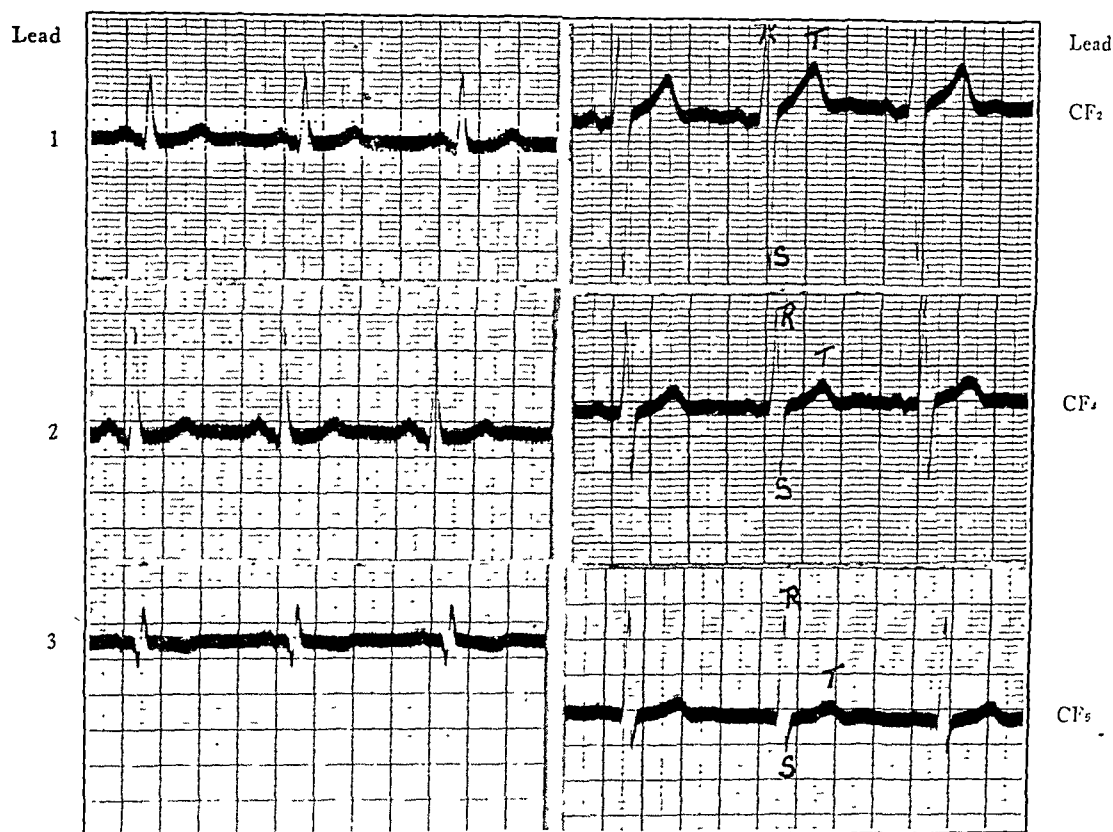


FIGURE 6. Normal Electrocardiogram.

Normally, in Lead CF_2 (Fig. 6), there tend to be a small R, a deep S and an upright T, which, however, may be fairly low. The P wave is unimportant, since it may be upright, inverted or diphasic. In Lead CF_4 , R and S are frequently equal and there is a fair excursion of each. T is normally upright. In Lead CF_6 , R becomes higher and S shorter in the average normal and T continues to be upright but is lower. It is only in Lead C_1 that T may be inverted normally in the adult; in young children one may find that the normal precordial T wave is inverted.

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MISCELLANY

MILITARY AWARD TO DR. LYONS

Major Champ Lyons, M.C., A.U.S., associate in surgery and instructor in bacteriology and immunology, Harvard Medical School, and assistant surgeon, Massachusetts General Hospital (on leave of absence), has recently been awarded the Legion of Merit because, according to his citation, "he initiated and guided the methods by which the new and potent agent penicillin has been utilized in the treatment of the seriously wounded." His citation continues: "From the most forward mobile hospitals of Italy to the large general hospitals of the Interior, he personally operated upon and studied the treatment of the wounded, instructing his seniors and subordinates alike in a change of surgical procedures which is productive of better results. Lives and limbs of soldiers have been saved, and the disability and deformity of wounds materially reduced. His professional judgment, combining a basic knowledge of the science of bacteriology with skill and experience in practical surgery, has cast new light on the age-old problem of wound surgery. At no time has he spared himself mentally or physically, and the example he has set is an inspiration to all surgeons in the service."

MILITARY AWARD TO DR. MOORE

Major Merrill Moore, M.C., A.U.S., former associate in psychiatry at the Harvard Medical School and the Boston City Hospital, has been awarded the Bronze Star Medal by Major General O. W. Griswold, commanding officer of the Fourteenth Army Corps. This award made by direction of the President, reads: "For meritorious achievement in connection with military operations against the enemy in the South West Pacific."

In recommending Major Moore for this citation, his commanding officer said specifically:

Your service at this base has been of the greatest benefit to the Government and to our war effort. Facing an immense problem, in your energetic and ingenious manner, you rapidly reduced the obstacle of psychoneurosis and related disorders in this area. As the only psychiatrist at that time, you immediately set about your assigned tasks with complete disregard for personal comfort and safety in your effort to solve existing difficulties. In addition to your regular hospital duties you devoted your personal leisure to consultations and lectures to all unit officers in this organization, often flying long distances to do so, so that they could understand and properly assist soldiers with emotional disturbances.

Of the large number of cases called to your attention by line officers or referred to you for diagnosis and treatment by medical officers, a remarkably high percentage were returned promptly to effective duty and the majority of the remainder were returned shortly thereafter. In doing this you were always efficient, sympathetic, reasonable and constructive.

Your performance of duty has been exceptionally meritorious. You have been a decided influence on the morale of our forces and an inspiration to the men with whom you have worked. You have strengthened co-operation and you have established confidence among officers and enlisted men as to the effectiveness of preventive psychiatry in the field as well as the value of mental hygiene for combat troops. Your actions contributed materially to the success of our combat operations.

NOTE

The following appointments to the teaching staff of Harvard Medical School have recently been announced: James Blanding Arey, of Minneapolis, Minnesota (S.B. University of Minnesota 1935, M.B. 1937, M.D. 1938 and S.M. 1940), instructor in pathology; Richard Colbert Cecil of Richmond, Virginia (A.B. Emory and Henry College 1925, M.D. Medical College of Virginia 1932), assistant in medicine; George Constantin Cotzias, of Canaan, Greece, now working at the Massachusetts General Hospital, Boston (M.D. Harvard University 1943), assistant in neurology; Peter Hugh Forsham, of New York City (B.A. University of Cambridge 1937, M.A. University of Cambridge 1941, M.D. Harvard University 1943), research fellow in medicine; Lee Nathaniel Foster, of Oak Park, Illinois (S.B. Northwestern University 1938, M.B. 1940, M.D. 1942), assistant in pathology; George Erwin Gutmann, of Chapel Hill, North Carolina (M.D. University of Louisville 1943), assistant in pathology; David Milford Hume, of Muskegon, Michigan (S.B. Harvard University 1940, M.D. University of Chicago 1943), assistant in surgery; Edith Meyer, of Jamaica Plain (Ph.D. University of Leipzig 1933), research fellow in pediatrics; Robert Durant Ray, of Berkeley, California (A.B. University of California 1936, A.M. 1938, M.D. Harvard University 1943), assistant in orthopedic surgery; Eli Robins, of Rosenberg, Texas (A.B. Rice Institute 1940, M.D. Harvard University 1943), assistant in psychiatry; Daniel Sciarra, of Paterson, New Jersey (A.B. Harvard University 1940, M.D. 1943), assistant in neurology; Paul John Votta, of Providence, Rhode Island (A.B. Brown University 1936, M.D. Boston University 1941), assistant in roentgenology; and Philip Hulet Walker, of Minneapolis, Minnesota (S.B. Harvard University 1939, M.D. 1943), assistant in surgery.

BOOK REVIEWS

An Atlas of Anatomy. Vol. 1. Upper limb, abdomen, perineum, pelvis and lower limb. By J. C. Boileau Grant, M.C., M.B. Ch.B., F.R.C.S. (Edin.). 4^o, cloth, 214 pp., with 227 illustrations. Baltimore: Williams and Wilkins Company, 1943. \$5.00.

Those familiar with the author's *Method of Anatomy* (Baltimore: Williams and Wilkins Company, 1940) will not be surprised that this first volume of an atlas of anatomy, devoted to the upper limb, abdomen, perineum, pelvis and lower limb, is characterized by originality of approach and treatment and by perfection of technic. The 227 illustrations, of which nearly half are in two or more colors, are made from enlarged photographic positives of actual dissections, traced and then worked up by a competent artist. They are unusually lucid and true, and free from the confusion of too much detail. The labeling of structures is clear; the text intentionally slight. It is intended that the student should use Dr. Grant's *Handbook for Dissectors* and refer to the *Method of Anatomy* mentioned above for description and comment. When the second volume of the atlas shall be issued, this group of books may be heartily commended to student and practitioner alike.

An Introduction to Group Therapy. By S. R. Slavson. 8^o, cloth, 352 pp. New York: The Commonwealth Fund, 1943. \$2.00.

In the author's words, this volume "deals with a method of psychotherapy employed at the Jewish Board of Guardians of New York since 1934 and known as Group Therapy." The board serves underprivileged city children, boys and girls, who present "problems of personality" of the sort that "may manifest themselves in the form of delinquent or neurotic behavior." Service is rendered to boys and girls up to the age of eighteen.

Among these children, the majority of those who are selected for group therapy are under fourteen and apparently none are under eight years of age. Each therapeutic group consists, ideally, of five to eight children, who meet periodically with an older person known technically as the "group therapist." By their members the groups are called "clubs," and this word adequately suggests the spirit in which the meetings are conducted.

The book offers a comprehensive and detailed exposition of the practical and executive problems presented by such therapy. Emphasis is placed on the close and successful integration of group therapy with other social-service activities and with individual psychotherapy, including even individual child analysis. The presentation contains many excellent case histories and many vivid play-by-play accounts of what has occurred in specific group meetings.

The theoretical point of view that synthesizes and directs this wealth of otherwise probably bewildering and inchoate details and activities appears to be strongly and even predominantly psychoanalytic. This is apparent not only in the general orientation of the book but also in the use and even definition of specific terms. Thus one meets repeatedly the words "super-ego," "transference" and, less exclusively psychoanalytic, "ego," and one reads that "the chief charac-

others find too slow or too fast, and they determine and maintain the standard at which medical education should be conducted. They have been hard pressed by the accelerated curriculum, but they have risen to the occasion and are responsible for whatever success has attended the project.

But there is a time factor in the educational process for which even the stimulus of war cannot compensate. The physicist, the chemist, the physiologist, the pathologist, the clinician, all take account of time in their scientific and practical calculations. So the educator might devise some such formula as $(c + r + e)t$ to designate the quality of his product, c being the intellectual capacity of the student, r the resources of the school attended, e the effort devoted to the educational process by both the student and the faculty, and t the time during which these processes are in operation. Whatever the formula or the philosophy, time is an inevitable element.

The facts that formerly most medical students devoted some — and a few, all — of their summer vacations to medical pursuits, that the members of the faculties, because of diminishing numbers, have had to give even more time to teaching than that demanded by the nine-month year and that a nine-month internship does not meet the minimum requirements mean that the quality of medical education, other things being equal, must have deteriorated during the wartime acceleration of the curriculum. It was an emergency device, — “any port in a storm,” — but it now appears that the storm has passed sufficiently for us to clear our decks again and to make our ship as stout and as seaworthy as possible. We are now planning to train the doctors of 1949 and later.

Are we to train them at the highest possible level and to meet the national and international responsibilities that we are now assuming? Before this question can be answered the time elements involved in the accelerated programs of our medical schools must be thoughtfully scanned by the medical, military and educational authorities of the Nation. The simplest method of deceleration would be to return to the annual type of curriculum and simultaneously to extend the 9-9-9 into a 12-12-12 plan for hospital internship. In the natural course

of events this would bring about a gradual, not a sudden, return toward normal. If these changes were to be made effective as of June, 1945, the future classes to graduate from our medical schools would have the following medical-school increments, including vacations: Class of 1945, thirty-six months; Class of 1946, thirty-nine; Class of 1947, forty-two; and Class of 1948, forty-five. Furthermore, each graduate would have at least a twelve-month internship.

Continuation of the nine-month curriculum beyond June, 1945, can be justified only by two considerations: first, that there are values in the accelerated program that should be projected into peacetime and, second, that the national emergency is still acute enough to sacrifice quality for quantity in medical-school output in 1948 and 1949. Furthermore, if the latter consideration does hold, it seems likely that both the Army and the country in general would be benefited if the required number of physicians were obtained by increasing the percentage of Army matriculants rather than by retaining the accelerated schedule.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DION — Thomas J. Dion, M.D., of Quincy, died November 27. He was in his seventy-seventh year.

Dr. Dion received his degree from Laval University Medical Faculty, Montreal, in 1891. He was the oldest member of the Quincy City Hospital staff and had served as health commissioner and city physician in Quincy. He was a member of the American Medical Association.

His widow and a son survive.

O'NEIL — Richard F. O'Neil, M.D., of Boston, died November 30. He was in his seventy-first year.

Dr. O'Neil received his degree from Harvard Medical School in 1897. During World War I, he was commissioned a captain in the Medical Corps, serving as assistant to the surgeon-in-chief of the Department of Urology at Base Hospital No. 6 in France. He was promoted to major in 1918, and honorably discharged the following year. For several years he was private assistant to the late Dr. William M. Conant, outpatient surgeon at Carney Hospital and visiting surgeon at St. Elizabeth's Hospital. In 1911 he was appointed genitourinary surgeon in the Out Patient Department at the Massachusetts General Hospital. He was named visiting surgeon of the Genitourinary Service in 1915, and became chief of the service in 1917. He served as associate urologist at the Massachusetts General Hospital until 1934, when he was appointed to the board of consultation after reaching retirement age. He was well known at Harvard Medical School, where he was a member of the teaching staff. He was a member of the Boston and New England surgical societies and the American Medical Association and a fellow of the American College of Surgeons. He was a member of the American Urological Association, of which he was president from 1927 to 1928, as well as of the New England Section of the American Urological Association and the American Association of Genitourinary Surgeons, both of which he had served as president and secretary.

His widow and a son survive.

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Since the book covers the major research work done on the subject during the past ten years, it should be of considerable value to research workers.

Aesculapius in Latin America. By Aristides A. Moll, Ph.D., secretary-editor of the Pan-American Sanitary Bureau, Washington, D.C., and consultant in tropical medicine to the Secre-

teristic of the therapy group is its similarity to the family" and that the group therapist's, much like the psychoanalyst's, "chief function is to be a *neutral* person so that each . . . member of the group projects on the therapist his unconscious attitude toward adults."

On Growth and Form. By Sir D'Arcy Wentworth Thompson, 8°, cloth, 1116 pp., with 555 illustrations and frontispiece. New York: The MacMillan Company, 1943. \$12.50.

This famous and monumental monograph, written during World War I and first published in 1917, has been out of print and extremely scarce for the past twenty years. The present edition has been revised and enlarged by its distinguished author as a *solacium ac perjugium* when active service was debarring him by his years. Much new material has been added. The chapter on rate of growth is double its original length; and the subjects of the bee's cell, the radiolarian skeleton, the mechanical construction of a bird, and Galileo's principle of similitude have been much extended. So unbounded is the writer's range of knowledge that scarcely any subject in biology is untouched. There is discussion, for example, of the fascinating problem of the left-handed snail shell and of the tetrakaidekahedral shape of cells in cell-aggregates, first noted by Joseph Plateau and Lord Kelvin and so beautifully demonstrated in this country by Dr. F. T. Lewis, of the Harvard Medical School.

Sir D'Arcy Thompson is a man of science who writes like a novelist; all the charms and merits of literary excellence and style are his. Moreover, so vast is his erudition that his volume is a treasury of apposite classic allusion and universal scientific reference. It is a work of perfect, total and utter scholarship, wherein the author, like Henri Fabre, the old man eloquent to whom he refers, "in his all but secular life has tasted of the first fruits of immortality."

Civilization and Disease. By Henry E. Sigerist, M.D., D. Litt., LL.D., 8°, cloth, 255 pp., with 52 illustrations. Ithaca, New York: Cornell University Press, 1943. \$3.75.

The part played by disease in determining the progress and even the form of civilization is the fascinating subject that Dr. Sigerist discussed in the Messenger Lectures for 1940 and that he has further expanded in this delightful volume. Civilization is first presented as a factor in the genesis of disease, and in subsequent chapters, the relation of disease to economics, social life, law, history, religion, philosophy, science, literature and art is studied. Not less valuable than the factual matter are the glimpses that the reader gets of the author's philosophic assay of conditions and factors that, through the ages, have brought the world to its present pass, and he will be comforted by a final declaration: "The more I study history, the more faith I have in the future of mankind. . . . While we are struggling, the foundations are being laid for a new and better civilization."

The volume is excellently turned out, and is embellished by many beautiful reproductions of treasures from the world's museums. An excellent index gives quick guidance, whether one's interest be in "worms" or "Hitlerism."

Many a reader of this volume will find difficulty in laying it down unfinished, and will long for the leisure to browse among the sources of the allusions and references that are so lavishly spread before him.

Female Endocrinology. By Jacob Hoffman, M.D., 8°, cloth, 780 pp., with 180 illustrations. Philadelphia: W. B. Saunders Company, 1944. \$10.00.

This book is an able exposition of the accumulated knowledge of endocrinology as it pertains to women. The book is really more than a review of female endocrinology, since it contains chapters on all the endocrine glands, in their relation not only to female physiology and pathology but also to general body physiology. This constitutes the reviewer's main criticism. To explain the mechanism and workings of all parts of the body a volume many times larger than this is needed, and in a book dealing with female endocrinology the pertinent relation of the nongenital glands to the genital glands should be sufficient. As a reference book it is good, since nearly all the important work of the last fifteen years has been included. Like all books on such a rapidly changing subject it cannot keep up with the times.

The careful explanation and the actual description of the technics for hormone determinations will be valuable to all workers in the field, especially those in laboratories in which such tests have not been performed. In the opinion of the reviewer this book is an excellent and able work on female endocrinology, but it should always be recognized that such a book is far from definitive.

Clinical Lectures on the Gallbladder and Bile Ducts. By Samuel Weiss, M.D., 8°, cloth, 504 pp., with 125 illustrations and 21 tables. Chicago: The Year Book Publishers, Incorporated, 1944. \$5.50.

This is a nicely dressed book, well printed and well illustrated. It discusses diseases of the gall bladder and bile ducts in a series of twenty-nine clinical lectures. The method of approach makes for easy reading, introducing a certain degree of informality that is pleasant. At the end of each lecture is a bibliography, placing at the reader's disposal a great deal of pertinent modern literature. On the whole the volume is by no means exceptional, but on the other hand covers its subject adequately and in a practical manner that may appeal to many readers.

Handbook for the Medical Secretary. By Miriam Bredow. First edition. 8°, cloth, 253 pp., with 18 illustrations. New York: McGraw-Hill Book Company, Incorporated, 1943. \$2.25.

Miss Bredow has produced an excellent handbook to be used as a guide to the conduct of a medical secretary or assistant. It deals with general information peculiar to the physician's office: patients, their records, filing, handling of appointments, accounts, correspondence and office procedure. The author also has included a brief description of various specialties of medicine, suggestions concerning the preparation of scientific manuscripts and a summary of the relation between the doctor and the law. A glossary of 2000 medical terms appears at the end.

If used with intelligent application, not as an irrevocable authority, this book will fill a much needed place as a textbook for the teacher and student of medical secretarialship as well as a reference book for those already holding such positions. It would be impossible for one small volume to be all inclusive since each chapter could overflow easily into a separate monograph and there is no vocation where such a variety of methods and experiences may be encountered as that of medical secretary.

Osler's Principles and Practice of Medicine. By Henry A. Christian, A.M., M.D., LL.D., Sc.D. (hon.), Hon. F.R.C.P. (hon., Can.). Fifteenth edition. 8°, cloth, 1498 pp. New York: D. Appleton-Century Company, Incorporated, 1944. \$9.50.

The fifteenth edition of *Osler's Principles and Practice of Medicine* is off the press. In appearance and general make-up it follows previous models; the chief difference is that it is more Christian and less Osler than heretofore.

When medical textbooks are discussed, two divergent viewpoints are apparent: one claims that no single person can know enough of medicine to compose a useful book that is properly inclusive, and the other that one writer of wisdom and broad experience, particularly if he happens to be an assiduous student of medicine with an adroit pen, can produce a volume that is fully as informative, more evenly written and better balanced in use of space or material than any developed through polyandry.

This reviewer confesses that he belongs to the latter school. Thus he has enjoyed succeeding editions of *Osler*, — in part because of the very fact that they were written by one author, — always finding each one refreshing, agreeable to study and serviceable. The fifteenth is no disappointment.

Those who have been brought up on *Osler* will appreciate the ease with which the book can be read — a tribute to Dr. Christian's ability to carry on the Oslerian tradition as a writer; the references to pertinent literature, which come at the end of each section and are amazingly up to date — a tribute to Dr. Christian's ability to extract the meat from periodical literature as it accumulates; and the index at the end by which any topic from abasia to zinc poisoning can be located without difficulty — a tribute to good bookmaking.

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THE USE OF SULFADIAZINE AS A PROPHYLACTIC AGAINST RESPIRATORY DISEASE*

CAPTAIN RICHARD G. HODGES, M.C., A.U.S.

DURING the winter season of 1942-1943, an Army Air Force technical school, located in the midwestern part of the country, experienced a severe epidemic respiratory disease. Waves of streptococcal sore throat and pneumococcal pneumonia struck the post in mid-February, 1943, and these diseases persisted at high levels until the end of May. During January, 1944, the rate for streptococcal sore throat again rose to a high level, reaching 6.0 admissions per 1000 men a week; at the same time, the incidence of lobar pneumonia rose to 5.6 admissions per 1000 men a week. It appeared that the epidemics of the previous winter were about to be repeated, and the decision was made to try the prophylactic effect of sulfadiazine.

METHOD OF INVESTIGATION

The technical school furnished an ideal population for investigation. The school is divided into two teaching shifts, each composed of approximately 1000 men. The general environment, the living conditions, the duties and even the recreations of the two groups are identical. The shifts are on different time schedules, so that mixing between the two is minimal. During the period of observation, the percentage distribution according to length of service, that according to duration of stay on the post and that according to age were calculated for each of the groups; no significant differences were found. The inflow of new troops into the groups was determined and was also found to be closely similar for the two. Finally, respiratory disease had been carefully followed in the school for many months and at all times the component units had shown a closely similar trend in disease rates.

The sulfadiazine pills were distributed by the squadron command. Each man admitted to the hospital was asked whether he had taken his pills, and numerous statements were obtained concerning how consistently the medication was being taken. It is estimated that for a given day 15 per cent of the men failed to take pills owing to having

days off, being on work details or failing to cooperate. In this respect, no single squadron appeared to be worse than the others. During a three-day period following each administration of the drug, corrections were made for men admitted to the hospital who had failed to take the pills when they were supposed to, 28 such patients being dropped from the series under study.

Hospital admissions were used to score the results. Attendance at sick call was not tabulated, but estimates of its volume were obtained from dispensary officers and in all instances paralleled the experience with hospital admissions. Each patient admitted was followed on the ward until the diagnosis was established, and his chart was checked following discharge.

The cases were classified as follicular tonsillitis, lobar pneumonia, atypical pneumonia and ordinary respiratory disease. The diagnosis of follicular tonsillitis was made in the presence of pharyngeal edema with exudate. Thirty per cent of the cases were cultured. Of these, 92 per cent were positive for beta-hemolytic streptococci, 3 per cent were positive for pneumococci, and 5 per cent were negative. From this it was concluded that follicular tonsillitis was an indication of streptococcal infection. Lobar pneumonia was identified by its clinical picture and by x-ray examination. Pneumococci were typed from 75 per cent of the cases. Atypical pneumonia was distinguished by its clinical picture. The remaining cases, classed as ordinary respiratory disease, included rhinitis, pharyngitis, laryngitis and acute bronchitis.

RESULTS

Effect on total respiratory disease. Figure 1 shows the response of admissions for all types of respiratory disease to the administration of sulfadiazine. On February 2, 3 and 4, 1944, members of Teaching Shift A received 2 gm. a day. The admission rate of the group promptly fell and for ten days remained between one third and one half that of the control group. On February 18 and 19, members of Teaching Shift B received 2 gm. a day. The

*From the Army Air Force Rheumatic Fever Control Program

teristic of the therapy group is its similarity to the family" and that the group therapist's, much like the psychoanalyst's, "chief function is to be a neutral person so that each . . . member of the group projects on the therapist his unconscious attitude toward adults."

On Growth and Form. By Sir D'Arcy Wentworth. Principally 8°, cloth, 1116 pp., with 555 illustrations scattered throughout. New York: The MacMillan Company, 1944. Appended to the text—

This famous and monumental monograph in Latin America and World War I and first published (1492 to 1943). A bibliography and extremely scarce indices of names and subjects present edition has been is an essential text for all libraries, distinguished author as, and for all historians.

service was debarred. *Methods of the United States Army.* Edited by original les. Simmons, M.D., Ph.D., D.P.H., Sc.D. (hon.), larian,adier general, M.C., U.S.A., chief of the Preventive Medical Service, Office of the Surgeon General, lecturer, Department of Preventive Medicine, Johns Hopkins University School of Medicine, lecturer in public health, Yale University School of Medicine, professorial lecturer in preventive medicine, George Washington University Medical School, and lecturer in tropical medicine, Army Medical School; and Cleon J. Gentzkow, M.D., Ph.D., colonel, M.C., U.S.A., and commanding officer, Deshon General Hospital, Butler, Pennsylvania. Fifth edition. 8°, cloth. 823 pp., with 103 engravings and 8 color plates, Philadelphia: Lea and Febiger, 1944, \$7.50.

This composite work was first published as *Medical War Manual No. 6* and was written during World War I by officers of the United States Army. Since that time the manual has passed through four editions and has been enlarged at each appearance. This fifth edition has been revised throughout to bring it thoroughly up to date; many sections have been completely rewritten.

Guiding the Normal Child. By Agatha H. Bowley, Ph.D. With a foreword by D. R. MacCalman, M.D., Crombie-Ross Lecturer in Psychopathology, University of Aberdeen. 8°, cloth, 174 pp., New York: Philosophical Library, 1943, \$3.00.

This small book describes the normal growth and development of children from birth to adolescence; it is of a popular character and designed for all persons interested in child guidance and the proper growth of children, and should be of interest to physicians. Emphasis is placed on the psychological aspects and on the development of personality. The manual is divided into four periods of a child's life: infancy, preschool period, the middle years of childhood and adolescence. A chapter on children and the war concludes the volume.

The Letters of Doctor George Cheyne to Samuel Richardson (1733-1743). Edited, with an introduction, by Charles F. Mullett, Ph.D., professor of history, University of Missouri. Vol. XVIII. The University of Missouri studies: No. 1. 4°, paper, 137 pp., with 4 illustrations, and frontispiece. Columbia, Missouri University; University of Missouri, 1943.

This monograph reproduces eighty-seven letters written during the period 1733 to 1743 and copied into a notebook owned by Samuel Richardson and now in the University of Edinburgh library. The existence or whereabouts of the original letters are unknown. This work should be of interest to historians of medicine and should be added to history collections in medical libraries.

Rorschach's Test. Volume I: Basic Processes. By Samuel J. Beck, Ph.D., head of the Psychology Laboratory, Department of Neuropsychiatry, Michael Reese Hospital, Chicago, and associate professor of psychology, Northwestern University. With a foreword by Willard L. Valentine, Ph.D., head of the Department of Psychology, Northwestern University. 8°, cloth, 223 pp. New York: Grune and Stratton, 1944. \$3.50.

The intent in the present volume is to demonstrate the processes used in evaluating responses to the Rorschach test. The sole purpose is to provide students with a moderately steady frame of reference, with the hope that given such a manual of constant usage it will be possible to work with the test as a stable instrument.

Medicine Annual—1943. 8°, cloth, 659 pp., with 100 illustrations. Minneapolis: Modern Medicine, 1944.

This is a collection of abstracts in all fields of medicine and surgery, which are brought together for convenient reference. All were originally published in the periodical, *Modern Medicine*. They are grouped by subject. The latest developments in the use of penicillin, sulfonamides, hormones and vitamins are discussed. The newer procedures in the diagnosis and treatment of cardiac and gastrointestinal disorders are considered, as well as techniques in every phase of surgery and orthopedics. There is a special division on military medicine and surgery in its various aspects, comprising thirty-two articles. The abstracts are short and well condensed, and provide a review of practical medicine and surgery as seen by the specialist in 1943. This manual should prove useful for ready reference purposes and should be in all medical libraries.

The Principles and Practice of Medicine, Originally written by Sir William Osler. By Henry A. Christian, M.D., LL.D., Sc.D. (hon.), F.R.C.P. (hon.) (Can.), clinical professor of medicine, Tufts College Medical School, and visiting physician, Beth Israel Hospital, Boston. Fifteenth edition. 8°, cloth, 1498 pp. New York: D. Appleton-Century Company, Incorporated, 1944.

This edition has been revised to place in the hands of the medical practitioner and Army and Navy personnel the most recent information brought to light since the publication of the preceding edition in 1942. Special emphasis is given to infectious and venereal diseases, tropical medicine and food deficiency disorders.

Textbook of General Surgery. By Warren H. Cole, M.D., professor and head of the Department of Surgery, University of Illinois College of Medicine, and director of Surgical Service, Illinois Research and Educational Hospitals, Chicago; and Robert Elman, M.D., associate professor of clinical surgery, Washington University School of Medicine, assistant surgeon, Barnes Hospital, associate surgeon, St. Louis Children's Hospital, and director of Surgical Service, H. G. Phillips Hospital, St. Louis. Fourth edition, 8°, cloth, 1118 pp., with 559 illustrations. New York: D. Appleton-Century Company, Incorporated, 1944. \$9.50.

The first edition of this book was published in 1936 and it was thoroughly revised in 1941. This fourth edition has been brought up to date by the inclusion of new material throughout the text. New pages have been added to include more data on fluid and electrolyte balance of amino-acid therapy, hypoproteinemia, transfusion, chemotherapy and appendicitis. Increased emphasis has been placed on wounds, burns, surgical shock and other subjects related to war casualties. Despite the addition of new material the book has been kept the same size as the previous edition by the elimination of obsolescent material. A new chapter has been added, entitled "War and Catastrophe Surgery." Some of the illustrations have been improved and others have been replaced.

NOTICES

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

A meeting of the New England Ophthalmological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Tuesday, December 19.

At 7:30 p.m. there will be a demonstration of clinical cases followed by the business meeting. Drs. David Cogan and Morton Grant will then speak on the topic "An Unusual Type of Keratitis Associated with Exposure to Butanol," and Dr. Theodore L. Terry on the subject "Pathology of Eyes following Maternal German Measles." These will be followed by a paper "The Myopia Paradox" by Dr. S. Judd Beach, including a discussion opened by Dr. Walter B. Lancaster.

SOUTH END MEDICAL CLUB

A regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, December 19, at twelve noon. Dr. E. Everett O'Neil will speak on the topic "The Treatment of Venous Thrombosis and Embolism." Dr. Samuel Grossman will preside.

Physicians are cordially invited to attend.

(Notices continued on page xix)

pneumococci. In the ten months preceding the experiment an average of 30 per cent of the pneumo-

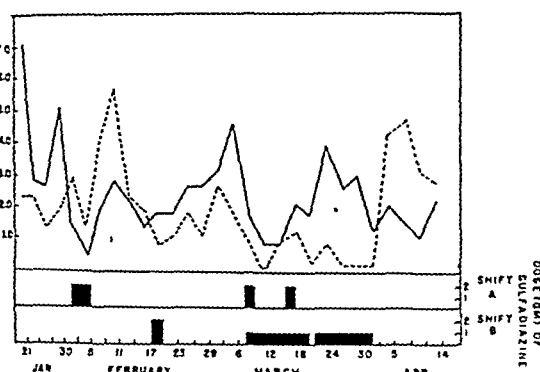


FIGURE 3. The Effect of Sulfadiazine on the Incidence of Lobar Pneumonia.

The solid line represents Shift A, and the dotted line, Shift B.

cocci typed were found to be Type 2. During the period of observation, this proportion rose to ap-

proximately 50 per cent. Increases in the proportion of Type 2 pneumococci could not, however, be correlated with the individual administrations of the drug.

Effect on ordinary respiratory disease. As shown in Table 2, the admissions for ordinary respiratory disease were affected in a manner and degree quite similar to those for pneumococcal infection. It has been suspected for some time that a fair proportion of the cases with this diagnosis were in reality bacterial infections. Beta-hemolytic streptococci and epidemic types of pneumococci were isolated from a number of these patients. It is presumed that this is the explanation for the effect of sulfadiazine but extensive laboratory work would be necessary to prove this point.

Effect on atypical pneumonia. Throughout the period of observation, the incidence of primary atypical pneumonia was low, being almost exactly one third that of pneumococcal pneumonia. This corresponded to the relatively low rate for ordinary

respiratory disease, it being the experience at this post that an average of 1 case of atypical pneumonia is admitted for every 10 cases of ordinary respiratory disease. The cases of atypical pneumonia were too few for significant analysis.

Effect on acute rheumatic fever. The streptococcus epidemics of streptococcal infection in 1943 and 1944 are contrasted in Figure 4. In the 1943 season, approximately eight weeks after the sharp February rise acute rheumatic fever appeared in epidemic proportions. In spite of the extremely high rates of January and February, 1944, no such outbreak of rheumatic fever appeared. This is demonstrated in Table 3, in which weekly rheumatic fever rates for the two years are compared, using the onset of the streptococcus epidemics as starting points. It should be borne in mind that although the 1944 curve of streptococcal infection appears to be continuous, it was in reality sharply broken for each group by the use of sulfadiazine (Fig. 2). It is not

TABLE 2. Effect of Sulfadiazine on Admissions for the Various Respiratory Diseases.

DISEASE	TIME INTERVAL	TEACHING SHIFT A		TEACHING SHIFT B	
		NO OF ADMISSIONS	AVERAGE ADMISSIONS PER DAY	NO OF ADMISSIONS	AVERAGE ADMISSIONS PER DAY
Ordinary respiratory disease . .	1/20-2/2	130	9.3	154	11.0
	2/3-2/18	85	5.3	169	10.6
	2/19-3/7	118	6.6	88	4.9
	3/8-3/19	46	3.8	33	2.8
	3/20-3/31	46	3.8	29	2.4
Lobar pneumonia	1/20-2/2	35	2.5	21	1.5
	2/3-2/18	22	1.4	33	2.1
	2/19-3/7	35	1.9	22	1.2
	3/8-3/19	12	1.0	6	0.5
	3/20-3/31	27	2.2	5	0.4
Streptococcal sore throat	1/20-2/2	49	3.4	60	4.3
	2/3-2/18	28	1.7	42	3.8
	2/19-3/7	84	4.7	60	3.3
	3/8-3/19	11	0.9	7	0.6
	3/20-3/31	26	2.2	8	0.7
Scarlet fever . .	1/20-2/2	8	0.57	10	0.86
	2/3-2/18	3	0.19	18	1.12
	2/19-3/7	12	0.67	7	0.39
	3/8-3/19	1	0.17	0	0
	3/20-3/31	5	0.42	0	0

ideal to compare the experience of one year with that of the next, but the results just cited suggest

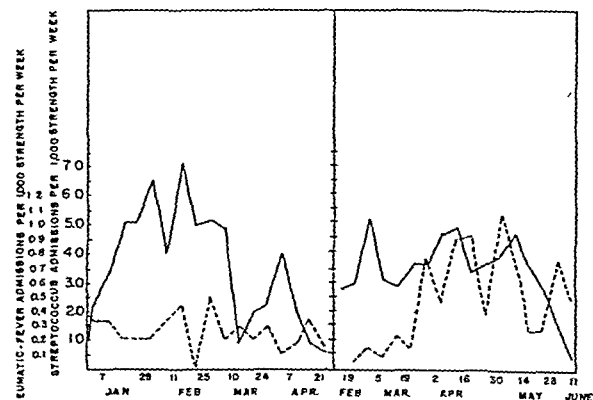


FIGURE 4. Comparison of Incidences of Streptococcal Infection and Acute Rheumatic Fever in 1944 (left) and 1943 (right). The solid lines represent streptococcal infection and the dotted lines acute rheumatic fever.

that sulfadiazine had a prophylactic effect on the development of acute rheumatic fever.

decrease in the admission rate was equally striking, but the duration of the effect was more transitory, lasting only four days. On March 7, the members of Teaching Shift B began to take 1 gm. of sulfadiazine a day. On March 8 and 9, and again on March 15 and 16, the members of Teaching Shift A received 2 gm. a day. Admissions from both groups fell sharply. The rate from Teaching Shift B remained low while the men were receiving the drug

Effect on pneumococcal infection. As was pointed out above, pneumococci were typed from 75 per cent of the patients with lobar pneumonia. Thus, the effect of sulfadiazine prophylaxis on lobar pneumonia admissions may be taken as a measure of its effect on pneumococcal infection. The effect of sulfadiazine prophylaxis is shown in Table 2 and Figure 3. The experimentation period is roughly divided into intervals of two weeks. In the periods follow-

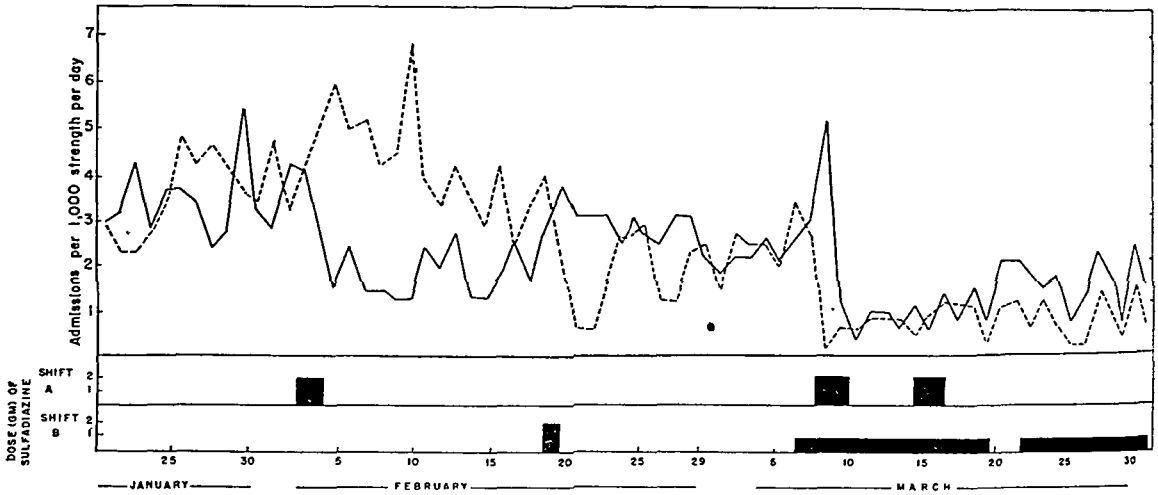


FIGURE 1. *The Effect of Sulfadiazine on the Incidence of Total Respiratory Disease. The solid line represents Shift A, and the dotted line, Shift B.*

daily. The rate for Teaching Shift A rose moderately five days after the second weekly treatment.

Effect on streptococcal infection. As might be expected, the most striking results were obtained with streptococcal sore throat or follicular tonsillitis (Table 1 and Figure 2). It is apparent that adminis-

ing the administration of the drug, the average daily number of admissions from the treated group fell; in the periods when no drug was given, it rose. Considering that the treatment periods included in

TABLE 1. *Effect of Sulfadiazine on Admissions for Streptococcal Sore Throat.*

TIME INTERVAL	TEACHING SHIFT A		TEACHING SHIFT B	
	NO. OF ADMISSIONS	ADMISSION RATE	NO. OF ADMISSIONS	ADMISSION RATE
1/1-1/7	11	2.5	8	1.9
1/8-1/14	13	2.9	17	4.0
1/15-1/21	22	4.8	24	5.2
1/22-1/28	20	4.2	29	6.1
1/29-1/31	12	5.9	10	4.9
2/1-2/3	12	6.0	18	8.9
2/4-2/6	6	3.0	16	8.2
2/7-2/9	2	1.0	15	7.8
2/10-2/12	4	2.0	15	7.6
2/13-2/15	8	4.1	20	9.7
2/16-2/18	7	3.4	17	8.2
2/19-2/21	17	8.1	3	1.4
2/22-2/24	11	5.3	9	4.3
2/25-2/27	13	6.2	7	3.1
2/28-3/1	12	5.8	12	5.7
3/2-3/4	8	3.8	15	7.2
3/5-3/7	10	4.7	14	6.7
3/8-3/10	13	5.9	3	1.4
3/11-3/13	3	1.4	0	0.0
3/14-3/16	3	1.4	4	1.9
3/17-3/19	1	0.5	1	0.5
3/20-3/22	5	2.3	1	0.5
3/23-3/25	5	3.6	2	1.0
3/26-3/28	5	2.3	1	0.5
3/29-3/31	8	3.6	3	1.4

tration of the drug reduced the incidence of this disease almost to zero.

Likewise, the response of scarlet fever to the medication (Table 2) was striking, the admissions dropping almost to zero.

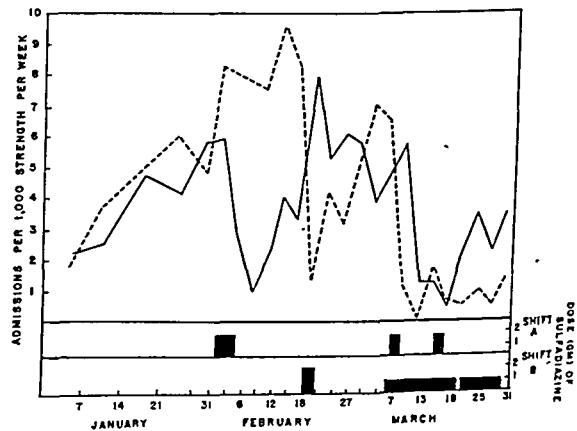


FIGURE 2. *The Effect of Sulfadiazine on the Incidence of Streptococcal Sore Throat. The solid line represents Shift A, and the dotted line, Shift B.*

tervals when the rates were returning to pretreatment levels, the results appear to be significant. It is possible that part of this reduction was due to the control of upper respiratory disease, resulting in a lessened dissemination of pneumococci.

Sulfadiazine failed to produce any clear-cut change in the distribution pattern of the various types of

THE PREVENTION OF PULMONARY EMBOLISM*

CHARLES A. ROBINSON, M.D.†

BOSTON

EVERY adult person who is confined to bed with illness — whether operative, medical, obstetric or traumatic — is a potential candidate for a pulmonary embolus. There is scarcely a physician who has not witnessed the sudden death caused when an embolus is propelled into the pulmonary artery from an unrecognized source. In such grave crises one is compelled to stand helplessly by the bedside, administering drugs futilely and almost at random in an attempt to bring the heart beat, blood pressure and respiration back to normal. Yet if preliminary observations are made and routine measures are taken, a large percentage of these deaths can be avoided.

No one knows for certain how many deaths are attributable to pulmonary embolism, but the mortality can best be appreciated if one considers the statistics of the pathologist. Barnes¹ writes:

According to Belt, pulmonary embolism was the cause of death in 6.5 per cent of 567 consecutive cases in which necropsy was performed on adults. McCartney reviewed 14,419 cases in which necropsy was performed on persons of all ages. In 9615 of these cases the patients had been treated medically; in the remaining cases the patients had died after operation, accident or obstetric delivery. Pulmonary embolism accounted for 2.72 per cent of deaths in this series. Collins reported 2.07 per cent of deaths from pulmonary embolism of 10,940 consecutive cases in which necropsy was performed at the Los Angeles Hospital. Subject to whatever selectivity such a series of cases represent, one can estimate that 34,000 people die of pulmonary embolism yearly in the United States. If such a percentage of deaths from pulmonary embolism is applicable to the general population, and unless this expectancy can be modified, it may be assumed that more than 3,000,000 people now living in the United States will eventually die of pulmonary embolism.

Great confusion exists among physicians regarding inflammatory diseases that attack the veins of the leg. Although it is true that all these diseases may be the precursors of pulmonary embolism, two of them — namely, thrombophlebitis of varicose veins and phlegmasia alba dolens, generally known as "milk leg" — rarely give rise to fatal complications, because in these diseases the thrombus is firmly attached to the vein wall. It must be pointed out that thrombophlebitis of varicose veins is an ailment of the superficial venous circulation, and can be easily diagnosed and successfully treated by ligation and division of the great saphenous vein and all its tributaries at the fossa ovalis. The swelling and pain of phlegmasia alba dolens can be successfully treated by novocain block of the lumbar sympathetic ganglions.

The type of phlebitis known as "phlebothrombosis" is far more dangerous than either of the diseases mentioned, and carries a much higher mortality. It is this malignant complication of the deep veins of the lower leg that gives rise to the vast majority of pulmonary emboli. Here they originate, lurking in the retarded blood stream and waiting to detach themselves either in whole or in part from the venous intima. If such detachment occurs, the clot is borne along the ascending venous circulation into the right auricle, and thence into the pulmonary artery and lung. At this point, either the patient suffers nonfatal embolism that produces an infarct of the lung or, if the entire thrombus tears loose and is of sufficient caliber, the pulmonary artery is blocked and death is a matter of minutes or even seconds. This disease entity is generally unobserved by the physician, and it is his tardiness or failure in detecting it that often leads to the much-dreaded pulmonary embolus. The following case is typical.

CASE 1. A 50-year-old, married woman was operated on for a panhysterectomy. Her recovery was seemingly uneventful until the 12th postoperative day, when she complained to the resident surgeon of pains and soreness in the left groin. When I questioned the patient, she admitted that she had noticed the pain 3 days previously in the left calf, but had not told the resident surgeon about it because she feared she would not be allowed to sit up. In the same period, the temperature and pulse had shown an unexplained rise. It should be noted that 3 critical days had elapsed since the appearance of the first symptoms.

Physical examination showed definite tenderness in the muscles of the left calf, with moderate swelling of the leg and a strongly positive Homans's sign. (To test for the Homans's sign the Achilles tendon is put on stretch by forcefully flexing the foot; where the sign is present, this manipulation causes pain in the calf of the leg.) There were tenderness and swelling over the femoriliac region, and slight cyanosis of the foot on dependency. (These constitute the classic signs and symptoms of late phlebothrombosis.) The symptoms were so obvious that venograms were not necessary.

An operation was immediately performed. The left femoral vein was opened under local anesthesia and a thrombus 18 cm. long, whose proximal end was non-adherent to the femoral vein and floating in the venous circulation, was removed. The right femoral vein was also opened, but no thrombus was found. The patient became ambulatory within 24 hours and was discharged on the 6th postoperative day.

In this classic case of late phlebothrombosis, one hesitates to surmise what would have happened if the symptoms had not been recognized and traced to their deepest significance, for it is cases like this that so frequently cause fatal pulmonary embolism. Actually, there was laxness in the precautionary routine of daily examination of the legs for the very signs and symptoms that were belatedly discovered.

Judging from the above case, phlebothrombosis may be misconceived as a highly dramatic and

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 24, 1944.

†Junior visiting surgeon, First Surgical Service, and chief of Varicose Vein Clinic, Carner Hospital.

Dosage. The least prolonged response to sulfadiazine was obtained by the administration on February 18 and 19 of 2 gm. a day to the members of Teaching Shift B. It is suspected that the shortness of this response may have been due to a heavy saturation of this group with streptococci during

nor was any depression of the blood-cell counts found. Patients with pneumococcal pneumonia who had received the drug prophylactically appeared to respond as well as ever to sulfadiazine.

SUMMARY AND CONCLUSIONS

During the month of January, 1944, hospital admissions for streptococcal and pneumococcal infections from an Army Air Force technical school rose abruptly and alarmingly. The experience of the preceding year suggested that serious and prolonged epidemics were beginning. The decision was made to try the prophylactic use of sulfadiazine, the organization of the school and the character of its component troops providing an ideal population for a controlled experiment.

Administrations of sulfadiazine were made throughout the months of February and March. In each instance the results appeared to be clear cut and beneficial. The most striking effect was on beta-hemolytic streptococcus infection. It appeared that streptococcal sore throat and scarlet fever could be reduced almost to zero. There was a less marked but still significant effect on pneumococcal infection. Sixteen weeks after the onset of the epidemic of streptococcal infection the incidence of acute rheumatic fever was well below the expected rate. Ordinary respiratory disease also showed a response to the drug. This is thought to be due to the fact that streptococci and pneumococci give a clinical picture indistinguishable from that of the common cold, although this concept remains to be proved.

A variety of dosages was tried. It is believed that the optimal dosage for a given group should be worked out individually.

No serious untoward reactions occurred.

TABLE 3. Comparisons of Admissions for Acute Rheumatic Fever in 1943 and 1944.

No. OF WEEKS AFTER ONSET OF STREPTO- COCCUS EPIDEMIC	1943		1944	
	NO. OF CASES	ADMISSION RATE	NO. OF CASES	ADMISSION RATE
1	0	0	3	0.34
2	1	0.07	2	0.22
3	2	0.15	2	0.21
4	1	0.08	2	0.22
5	3	0.23	3	0.33
6	2	0.15	4	0.43
7	10	0.78	0	0
8	6	0.46	5	0.51
9	12	0.90	2	0.20
10	12	0.92	5	0.30
11	5	0.38	2	0.20
12	15	1.19	3	0.30
13	10	0.76	1	0.10
14	5	0.38	2	0.18
15	5	0.38	4	0.35
16	10	0.76	3	0.25
17	6	0.46	2	0.16

the period February 2-16. The best response appeared to be from the prolonged daily administration of 1 gm. The data for March 7-19, however, indicate that there may be little to choose between this dosage and the administration of 2.0 gm. on two consecutive days once a week. It is believed that any given group represents a special problem in which a balance must be struck between economy in the use of the drug and an optimal therapeutic effect.

Untoward reactions. No serious reaction to the drug occurred during the period of observation. There were 2 moderately severe and several minor skin reactions. No renal symptoms were reported,

The literature clearly indicates that the maintenance of fluid balance is vitally important. This rationale is based on the fact that a dehydrated patient has a slower circulatory rate. It is imperative to keep a charted record of intake and output to maintain the fluid balance scientifically.

Since patients having varicose veins have been shown to be especially likely to develop superficial and deep phlebitis, it seems logical that if a patient has varicose veins they should be ligated, divided and injected before the fifth month of pregnancy, or prior to any elective operation. This comparatively simple treatment has been shown by many investigators to reduce the menace of pulmonary embolism. Warning must, however, be given that no varicose veins should be injected with a sclerosing solution without a preliminary ligation and division of the great saphenous vein. Failure to take this precaution has resulted in a number of deaths from pulmonary embolism.

Surgical trauma is a factor in causing phlebitis. Rough handling of tissues, leaning on the patient, especially over the femoroiliac region in abdominal operations, and poor approximation of tissues are possible contributory agents in failure to re-establish the normal venous return. For the same reason the holding of the legs is advisable in long gynecologic and obstetric operations are preferable to the use of stirrups. In addition, patients should also be out of bed and walking after a period of observation before the actual operation takes place. They should be made ambulatory by the third day after operation, especially elderly patients.

Many authorities, basing their conclusions on recent findings in biochemistry, look forward to the day when phlebitis will be prevented, or at least successfully treated, by the use of anticoagulant drugs. The medical literature is beginning to resound with claims made for heparin and dicoumarol,

both of which have the significant property of preventing the formation of blood clots. Barker, Allen and Waugh² report a series of 479 cases at the Mayo Clinic in which dicoumarol was used to increase the prothrombin time with a view to the prevention of pulmonary embolism. I have been unable to verify these results in my cases. There are so many contraindications to the use of this drug that it is perhaps unwise at the present time for the medical profession at large to employ it in the treatment of phlebothrombosis and thrombophlebitis. It apparently caused bleeding in ten per cent of the cases at the Mayo Clinic, and it cannot be safely used on patients suffering from blood dyscrasias, jaundice, hepatic disease and kidney complications. Heparin has the same end effects as does dicoumarol and is, in addition, much more expensive. The fact that it must be administered intravenously and that bidaily coagulation times must be obtained certainly does not enhance its attractiveness for general use at the present time.

* * *

Until such time as the anticoagulants have proved themselves to be safe and inexpensive drugs, the medical profession must depend on prophylactic measures, early diagnosis and surgery for the prevention of pulmonary embolism. This is a field in which the average physician, by simple routine expedients such as those described, followed by prompt utilization of surgery, can substantially reduce the mortality in cases of pulmonary embolism.

270 Commonwealth Avenue

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2. Barker, N. W., Allen, E. V., and Waugh, J. M. Use of dicoumarol [3,3'-methylenebis (4-hydroxy-coumarin)] in prevention of post-operative thrombophlebitis and pulmonary embolism. *Proc. Staff Meet., Mayo Clin.* 18:102-107, 1943.

easily diagnosed condition. Actually, the usual picture is quite the opposite. The early symptoms are obscure, indefinite and frequently overlooked. A considerable degree of diagnostic skill, together with routine daily examination of the lower extremities, is imperative if pulmonary embolism is to be avoided.

The following case illustrates an undramatic but undoubted case of phlebothrombosis in which we were fortunate enough to make an early diagnosis.

CASE 2. A 31-year-old multipara entered the hospital in moderate labor after an uneventful prenatal course. There was no history of varicose veins or previous phlebitis. Nine hours later she was delivered of a normal baby girl by spontaneous delivery, with a first-degree perineal laceration. The post-partum course was uneventful. The temperature and pulse remained normal for 7 days. The usual routine examination of the legs had been made each day, with no positive findings. On the 7th day, there were an unexplained temperature of 99.2°F. and a pulse of 94, accompanied by slight pain in the left calf. On surgical consultation there was moderate tenderness over the left calf muscles and a mildly positive Homans's sign. There was no swelling in the leg or cyanosis of the foot on dependency. It was suspected, however, that the patient had an early phlebothrombosis, and this was confirmed by venograms. Opening the femoral vein of the left leg revealed no thrombosis, and the usual ligation and division were performed. The right femoral vein was also opened. The postoperative course was uneventful, and the patient was discharged in 6 days.

Provided that a clot existed in the calf, the question arises whether if no femoral exploration had been made the clot would have spontaneously disappeared or would have resulted in embolus. The answer is not known but it is certain that the symptoms disappeared after the operation and that the danger of pulmonary embolism from this site was eliminated.

A patient may survive the initial embolus, but statistics prove that a second or third usually results in death. Obviously these emboli ascend from a deep phlebothrombosis. If disaster is to be avoided, either they must be surgically removed or the vein must be ligated and divided above the offending thrombus. Sometimes to get above the clot it is necessary to ligate as high as the inferior vena cava.

Occasionally a pulmonary embolus produces an infarct of the lung even before phlebothrombosis is recognized. This is a difficult diagnosis, requiring the keenest perception on the part of the physician. The following case illustrates an infarct that had been treated as pneumonia.

CASE 3. A 40-year-old man was discharged to his home from another hospital after convalescing from a supposed right lobar pneumonia. Three days after discharge he experienced a sudden sharp pain in the left side of the chest and coughed up blood. His physician diagnosed this as pneumonia in the opposite lung and put him to bed. The next day the patient experienced a severe pain in the left thigh and calf, which lasted for 17 hours. An internist was consulted and made a diagnosis of a pulmonary infarct, on the basis of the left lung and the swelling and tenderness of the right leg, together with a positive Homans's sign. The patient was taken to the Carney Hospital, where I confirmed the diagnosis of ascending phlebothrombosis of the femoral vein.

At an emergency operation the right femoral vein was found to contain a thrombus, fairly adherent to the vein wall, which was removed by instruments and suction. The left femoral vein was clear but was surgically divided routinely. The postoperative course was uneventful. The patient was out of bed within 24 hours and was discharged on the 10th hospital day. On the day before discharge x-ray examination of both lungs was negative.

There can be no reasonable doubt that this patient had developed a phlebothrombosis while lying in bed during the original illness. The correct diagnosis was completely overlooked by the patient's physician but was fortunately recognized by the consultant, who was familiar with the signs and symptoms of phlebothrombosis. Delay in operating might have resulted in a fatal embolism. There must be no waiting period after a diagnosis of phlebothrombosis has been made.

Seventy-two operations for exploration and division of the femoral vein have been performed at the Carney Hospital in the last two years, all demonstrating three cardinal lessons. The first is that phlebothrombosis usually occurs when the patient is lying in bed with the venous circulation retarded and the tone of the muscles relaxed. The second is that the diagnosis is frequently overlooked when the physician fails to make a routine examination of the lower extremities — especially the calves — during his daily ward rounds and neglects to note any unexplained slight rises in temperature and pulse. The third is that if phlebothrombosis is diagnosed, there must be no waiting period before surgical exploration of the veins. If these three principles are fully grasped, the mortality from pulmonary embolism is sure to be greatly reduced.

By this time it has become clear that pulmonary embolism rarely occurs unless some sort of phlebitis, usually phlebothrombosis, exists. The real prevention of pulmonary embolism therefore resolves itself into prevention of phlebitis. This can best be achieved by mandatory exercise of the lower legs, beginning immediately after the patient takes to his bed. It has been established that a close connection exists between the slowing up of the venous circulation and the formation of phlebothromboses. The object therefore is to accelerate the venous circulation by suitable exercises. An eminent physician has gone so far as to install bicycle pedals at the foot of the bed. This is effective but is impractical in a large hospital. The same beneficial result can be obtained by instructing the patient to simulate the pedaling motions of cycling. In my opinion a routine extension and flexing of the ankle and knee is just as effective. Something must be done to keep the venous circulation of blood at the normal rate. Under this heading come elevation of the legs in the Trendelenburg position for one hour twice daily, the use of nonconstricting abdominal dressings and routine deep-breathing exercises.

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FRANK BURR MALLORY*

A Doctor of Physicians

WILLIAM FREEMAN, M.D.†

WORCESTER, MASSACHUSETTS

The list of former orators of this society shows that never has a pathologist been honored in this manner. The laboratory man can now feel that he has been elevated from the group of "am-nots" to that select fraternity from which orators are chosen. I am deeply appreciative that you have given me the honor of being your orator on this occasion.

Very few if any of those present have not heard of Frank Burr Mallory. I venture to say, however, that very few know him as the physician and inspiring teacher that he was, and probably very few appreciate the tremendous influence his work had in lifting the practice of medicine from the treatment of symptoms to the more effective treatment of causes.

Dr. Mallory was born on November 12, 1862, in Cleveland, Ohio. His father, George Burr Mallory, was a sailor on the Great Lakes all his life, becoming in later years captain of his ship. His mother, Anna Faragher, was born on the Isle of Man, and it was largely through her influence and perseverance that her two children went to college. Eleanor, the daughter, became a schoolteacher. She is now retired and living in Florida. Frank attended the public schools of Cleveland and matriculated at Harvard College, where he earned his way by waiting on table in the dining hall. He was graduated with an A.B. degree at twenty-four years of age. He later attained an M.A. degree there, and in 1890 he received his M.D. degree. He paid his own way at medical school also, this time by doing technical work in the Department of Histology, a circumstance that undoubtedly started his interest in stains and histologic methods.

Immediately after graduation Dr. Mallory was appointed assistant in histology and had some sort of internship at the McLean Hospital, Waverley, where, from what can be learned, he spent most of his time feeding unco-operative patients by stomach tube. He then opened an office for the practice of medicine, but became discouraged when after several months without a single patient a young woman paid him an office visit for the express purpose of having an abortion performed.¹

In 1891 he embarked on his career. At about the same time Dr. William T. Councilman, newly selected Shattuck Professor of Pathology at the Harvard Medical School, was appointed pathologist at the Boston City Hospital. Dr. Mallory was made

Dr. Councilman's assistant, both at the medical school and at the hospital.

At that time the morgue and autopsy room at the Boston City Hospital were located in the boiler room on Albany Street, and the dead patients had to be carried from the hospital on a stretcher across this busy thoroughfare. This practice became so objectionable that it was decided to move the morgue and autopsy room to the hospital grounds. The singular choice of the second floor of the laundry building was made for these rooms, and although no public streets had to be crossed, the dead bodies had to be carried up a long, winding, narrow stairway.² Largely through the efforts of Dr. Councilman and Dr. Mallory, the city government finally agreed to the construction of a separate laboratory and mortuary building. When completed this structure was one of the most modern in this part of the country.

Shortly after this accomplishment, Dr. Mallory was married. He took his wife, Persis McClain Tracy, of Chautauqua, New York, to Europe for a honeymoon and spent it by working a year with Chiari in Prague and Ziegler in Freiburg. On his return in 1894 he was made an instructor in pathology at Harvard.

In 1896 came a series of far-reaching events. Dr. Mallory was promoted to assistant professor of pathology at the medical school, the new laboratory building at the hospital was formally opened, he was appointed first assistant to Dr. Councilman, and his first child, Tracy Burr Mallory, was born. The previous year Dr. J. Homer Wright had come from Baltimore and had been appointed second assistant to Dr. Councilman and assistant at the medical school. Dr. Mallory formed a lifelong friendship with Dr. Wright, and the two collaborated in many scientific and literary adventures. In 1900 another significant event occurred—a second son, George Kenneth Mallory, was born. A year later Dr. Mallory became an associate professor of pathology at Harvard. Dr. Councilman resigned in 1908 as pathologist at the hospital, and Dr. Mallory was appointed to that position. He later resigned from his teaching position at Harvard but became professor of pathology in 1928. In 1932, at seventy years of age, he became professor emeritus, as well as consulting pathologist at the Boston City Hospital.

Dr. Mallory received many honors during his lifetime, a telling reflection of the world-wide reputation he had attained in medical research. A brief list of these events is presented because they

*The annual oration delivered at the one hundred and fiftieth anniversary of the Worcester District Medical Society, April 12, 1944.

†Pathologist and director of laboratories, Worcester Hahnemann Hospital and Worcester State Hospital; instructor in pathology, Boston University School of Medicine.

testify to the significance that was attached to his work. He was an active member in many national medical societies and had been a moving force in the formation of several, among which were the American Association of Pathologists and Bacteriologists and the American Association for Cancer Research. He served as president and treasurer of the American Association of Pathologists and Bacteriologists, and until 1940 was editor-in-chief of its publication, the *Journal of Medical Research*, which later became the *American Journal of Pathology*. He was also elected an honorary member of the Pathological Society of Great Britain and Ireland and a corresponding member of the Royal Medical Society of Budapest. He was awarded the Ernst gold-headed cane of the American Association of Pathologists and Bacteriologists for specially meritorious work in pathology. He was the third man to be so favored by the society, the two previous awards having gone to William H. Welch and to Theobald Smith. Tufts College and Boston University each conferred on him the honorary degree of Doctor of Science. In 1935 he received the Kober Medal from the Association of American Physicians. He lectured by invitation before medical societies in many parts of this country.

In 1933, a year after his retirement, the City of Boston honored Dr. Mallory by erecting a modern laboratory building as a memorial to his untiring work and achievements. The Mallory Institute of Pathology at the Boston City Hospital stands today as a completely equipped institution for the study of pathology and for the training of men interested in this branch of medicine.

These are the high lights in Dr. Mallory's pervasive career in medicine. Although they serve for orientation, they no more than throw a hint concerning the import of his work. For a clearer appreciation of the latter one must probe deeper and study him in his varied works and interests.

Austerity is almost a requisite in people's mental picture of a scientist, and to those who did not know Dr. Mallory he appeared to be true to type.³ His credo was that the only way to do good work is to make that work an obsession and to avoid extracurricular activities, and since his pleasures were not such as to be related to social life, he seemed to others to live the life of an ascetic. He loved the outdoors and everything pertaining to life itself, however, — a characteristic that was probably inherited from his father. Early in life he developed an interest in botany, and nothing pleased him more than a tramp in the woods or a leisurely canoe ride when he would study the plants and flowers that he encountered. Almost every Saturday afternoon was devoted to these trips. He was a tennis enthusiast and could play a fast and scientific game. Whenever attending a match of professionals, he was more interested in their form

than in the score. When increasing age interfered with strenuous activities, he continued his daily walks, even up to a few months of his death. At home the early evening was often spent playing a piano duet with the elder of his sons. Such was the simplicity of living of this great man, a simplicity that allowed him extra time for work, for study and for thought.

It must be remembered that at the time Dr. Mallory began his professional career, scientific medicine, so called, was in its infancy. Illness was treated primarily according to symptoms, and there was little knowledge regarding the cause of the symptoms. Practically nothing was known about the tissue changes occurring in disease. The work of Pasteur and Jenner was known, but Virchow, the father of modern pathology, was in the midst of his labors, Koch was in the process of discovering the tubercle bacillus, Ehrlich was yet to discover salvarsan, and bacteriology was only approaching the heyday of its morphologic phase. With the great impetus given the search for causes by the success of investigators in bacteriology, it is probable that Dr. Mallory visualized the great need for studying the cause of disease so that it could be attacked directly rather than be treated on the basis of its symptoms alone. In studying the organs of a person who had died of a disease he visualized the immense opportunity that was afforded in helping his clinical colleagues treat and cure their patients more effectively. Cellular pathology was to him the key to the cause of disease, for it was in the cells, "the building blocks," that changes all the way from health to illness should be reflected. Given the proper tools, he believed that it should be possible to view the changes wrought in the cells, and from this it should be possible to reconstruct the destructive action and treat for it. But first tools were needed — highly sensitive tools. Here it can be stated that if Dr. Mallory had accomplished no more than his work on stains and histologic technics, he would still have been a great scientist, to such a high degree of perfection did he develop them.

It is probable that Dr. Mallory's early experience in the Department of Histology, while working his way through Harvard Medical School, created his first interest in the staining and fixing of tissues. He often reiterated that the perfect stain for the perfect section would reveal the basic essentials for the study of any disease, but conversely the imperfect stain and the imperfect section could only result in false observations and false conclusions. Mallory's staining and histologic technics, brilliant in conception and results, were developed only after tedious work and exhaustive experimentation. His experiments on this subject continued throughout his career. His work at the Boston City Hospital afforded him ample opportunity for improving and perfecting these technics and for demonstrating that they were usable in a routine laboratory. The

sheer wizardry that can convert a commonplace lesion stained by ordinary methods into a thing of beauty and distinction when put through one of his specific stains for cellular substances seems like a page out of a fairy tale.³

Of the more important discoveries he made in this connection are differential stains for *Endameba coli*, neuroglia fibers, collagen fibers, muscle tissue and connective tissue. He also developed methods for the detection of certain metallic poisons in tissue cells.

There arose a demand for a text on pathological methods, and in 1897 Dr. Mallory collaborated with Dr. Wright to publish the first edition of the now famous *Pathological Technique*,⁴ which has been the standard work on histopathology since its first appearance. It passed through eight editions and could be found on the bookshelf of almost every medical laboratory in America and Great Britain. After Dr. Wright died, it took many years before Dr. Mallory was finally persuaded to make another revision, the last edition appearing in 1938 and being dedicated to the memory of Dr. Wright. This book contains the most advanced and proved technics for fixing and staining any tissue in the human body and in any disease.

Nonetheless, to Dr. Mallory the correct preservation and staining of pathologic tissue was only a tool with which to study diseased cells. The intense urge to study the changes in tissue cells from the onset of a disease to its end drove him to persistent and tenacious work. In 1914 he published his great book, *The Principles of Pathologic Histology*,⁵ the result of years of experience and study. In the preface he stated that he was dealing with pathology from the morphologic standpoint and that his aim was to present the subject biologically, first by ascertaining the cells out of which various lesions are built, and then by tracing the development of the lesions from the simplest to the most complex forms so that at the autopsy or surgical table it could be read backward with some degree of certainty. As in all his publications, the text is liberally interspersed with beautiful drawings and photomicrographs in which the histologic pictures presented leave no one in doubt concerning the entities discussed.

At the turn of the century, when photography offered an advancement in pictorial delineation, Dr. Mallory was the first to use it in his publications. Characteristically, he studied and perfected photomicrographic technic until he was an expert. From then on all his publications were illustrated by exquisite photomicrographs. Furthermore, he insisted that all papers published in the journals of which he was editor be adequately and pertinently illustrated with the best photographs obtainable. Dr. Mallory often said that good photomicrographs should represent the perfect section, the perfect stain and the perfect microscopic field.

He further stated that he himself spent more time in selecting the section, the stain and the field than in writing the paper itself. Yet his sentences and phrases were also meticulously selected for simplicity and lucidity.

Mallory's hypothesis of cellular building blocks did not come out of thin air, a single case or a moment of armchair philosophy. In fact, he had an abhorrence of armchair theorists,⁶ and he insisted that each pathologist should base his theories only on careful study of the given disease in its many variations. In 1895 he himself started a study of the lesions of typhoid fever that was not completed until three years later. His published findings are as much an example of his careful and tenacious work and study as they are a classic report of the tissue and cellular changes pathognomonic of the disease so widespread in that day. Since at that time photomicrography was not yet known, he enhanced the clarity and comprehensiveness of his findings by a generous use of drawings of both the gross and microscopic lesions. So definitive was his study of the pathology of this disease that any well-trained pathologist can today diagnose a case of typhoid fever post mortem even though the causative bacterium has not been isolated.

Genius has been described as the infinite capacity for taking pains.³ Certainly Dr. Mallory's long and conclusive study of cirrhosis of the liver would qualify him as a scientist of surpassing genius even if it were the only work that typified his perseverance, the exactness of his technic and his thoroughness in exhausting all possible leads.

Cirrhosis of the liver was formerly a disease that was obscure in cause, more obscure in diagnosis and even more so in its nomenclature. Each type of cirrhosis was named after the particular writer who described a case or group of cases, and as Dr. Mallory later proved, most of these diseases were either the same type of cirrhosis or different stages of the same type. He believed that much was lost in studying the late stages of sclerotic liver disease, and hence he planned to study the onset and course. He expended more than twenty years of labor before he felt qualified to release his findings and give forth his conclusions. He first revealed that there are five distinct lesions from which cirrhosis can be derived. He then proved, with the aid of his differential stains, that hyalin is a pathognomonic finding of the liver-cell cytoplasm in so-called "alcoholic cirrhosis" of the liver. Then began his search for the cause of this type of disease.

In trying to find out whether addiction to alcohol did indeed produce cirrhosis of the liver, Dr. Mallory fed laboratory animals alcohol for many years. He finally concluded that ethyl alcohol per se is not the cause of alcoholic cirrhosis of the liver. Then followed years of painstaking work and disappointments in the search for the actual cause of this type of liver disease. Any less able man would have been

discouraged. When he believed that he could go no farther in his studies by the use of differential stains and cytologic methods alone, he resorted to animal experimentation. As new species of animal successively failed him, he tried another and still another. Finally, after nearly a quarter of a century of toil, he proved beyond all doubt that a certain type of cirrhosis of the liver can be caused by minute amounts of copper or phosphorus, but he was never able to explain satisfactorily the cause of alcoholic cirrhosis.

The abundant pathologic material from the South Department of the Boston City Hospital served as a basis for studies on the tissue changes in many contagious and infectious diseases, and it must not be supposed that Dr. Mallory neglected bacteriologic technics because of his fundamental, almost obsessive, interest in tissue studies. The bacteriologic and serologic technics used in his laboratories were the best and the most up to date, but they were used only as a means for rapid diagnosis and for proof of the etiology of the disease in which he studied the tissue changes. He contributed a chapter on the pathology of diphtheria to a book published by the Cambridge University Press, and made similar contributions on scarlet fever, measles and whooping cough. All cases coming to autopsy in his department received the same careful study and thought.

Dr. Mallory had to be sure of his ground before he published any findings. He meticulously followed all leads and considered all possibilities to determine which idea or ideas were tenable and which should be discarded. This sometimes led him into quite different byways; for example, his careful study of the cellular changes found in typhoid lesions led him to the discovery that endothelial leukocytes are phagocytic cells derived from the endothelium lining the blood vessels and vascular spaces. Although it is true that Metchnikoff's theory of phagocytes had been postulated some years before, it was from this that the true origin of Metchnikoff's macrophages was first learned, and it was from the results of his studies that Aschoff derived his concept of the reticuloendothelial system.

As the surgical removal of tissues and organs from the living body became more frequent, it was natural that Dr. Mallory spent more and more time and study on the cellular changes found in these specimens. His studies on the morphologic characteristics of neoplasms are another milestone in the advance of medical knowledge on this subject, for they resolved the confusion that was associated with neoplasms at that time. The current belief was that neoplastic cells were a sort of spontaneous and mysterious new life produced for its destruction of the host. The names attached to the various tumors found occurring in the human body were varied and meaningless, and oftener than not a

hitherto unpublished tumor had the discoverer's name attached to it. It is needless to point out the chaos inherent in such a situation. It was Dr. Mallory who by his characteristic methods of study proved that the cells of any tumor are derived from one of the three embryonic layers and that they thus have a definite histologic reference. From these findings he devised a system of nomenclature for neoplasms that was based on a firm scientific foundation and that could be understood the world over. These facts are not only of academic interest but also of the utmost clinical importance, for through them all the mystery regarding the origin of neoplasms was removed and it became possible to build an equally firm system of diagnosis and treatment.

The few studies described here in more or less detail are typical examples of the many adventures of Dr. Mallory in medical research. Whereas his contributions in the field of laboratory medicine are admitted by all to have been of outstanding and far-reaching importance, he himself was more concerned that his researches have significance to the clinician. That his investigations and findings should help other physicians in treating and curing disease was ever his immediate goal. He was among the first to recognize the need for studying the causes and symptoms of disease to derive practical clinical benefit therefrom. His contributions laid the foundation for the treatment of causes rather than of symptoms alone, and as such they are one of the greatest factors in the phenomenal advance of medicine in the last thirty years. They epitomize the change from an empirical to a scientific concept of medicine.

While Dr. Mallory was the pathologist of one large hospital and the consultant pathologist of many other hospitals, he was also the unofficial consultant to a great army of pathologists and clinicians throughout the world, and his diagnosis and opinion were always given freely, after careful study, and were devoid of self-conscious authority.

Aside from all these achievements, there was one aspect of his work that to Dr. Mallory meant more than all the others put together; this was his training of pathologists. On the commemoration of his fiftieth year after graduation, he wrote in his college yearbook, "Aside from the problems of my own work, one of my greatest pleasures has been in training young men and women in pathology and in seeing what they could make out of themselves under proper encouragement and stimulation; in other words, in getting them to do their own thinking and to work out their own salvation." Graduate physicians who came to study pathology with him found Dr. Mallory the inspiring teacher par excellence. To his students he gave all he had, and he attended to their training personally.

Severe in appearance and strict in his work though he was, Dr. Mallory was intensely human. In addition to his two sons, he had an army of

MEDICAL PROGRESS

SULFONAMIDE THERAPY IN OTOLARYNGOLOGY

ROBERT L. GOODALE, M.D.*

BOSTON

THE purpose of this review is to present the trend of thought in regard to sulfonamide therapy as it relates to otolaryngology. As a preface to the subject, attention should be called to two contributions that are helpful in evaluating the role of chemotherapy.

In a study of the outpatient records at the Massachusetts Eye and Ear Infirmary covering the five-year period 1937-1941, Richardson¹ records the clinical course of 645 cases untreated by sulfonamides. He charts the cases according to the bacteriology found at early paracentesis and to the duration of infection of those cases that did not go on to a surgical mastoid. In the cases in which hemolytic streptococci were found, he notes that 36 per cent did not heal until the fourth, fifth or sixth week. Cases with pneumococcal infection healed in an average of twelve days. In *Staphylococcus aureus* or *Staph. albus* infection the average duration of the discharge was ten days. In this series the incidence of mastoidectomy was as follows: hemolytic streptococcus, 10 per cent; pneumococcus, 4 per cent; and staphylococcus, 5 per cent.

Dean² reviews the literature of otitis media historically and presents figures from early authors regarding the mortality attending otitis media in the days before modern surgery and chemotherapy. He quotes Körner, who in 1902 published statistics for Prussia at the end of the nineteenth century and stated that from birth to ten years of age only 0.22 per cent of all deaths were attributed to otitis media. In the second decade 5.15 per cent, in the third decade 3.85 per cent, in the fourth decade 1.44 per cent and above forty years 0.27 per cent were otitic deaths. Dean writes that Bezold commented that these early statistics were actually too low because the pathologist usually did not examine every ear unless his attention was drawn to it. Dean quotes Dublin, statistician of the Metropolitan Life Insurance Company, to the effect that in 1940 in the United States the ratio of deaths due to ear infection to those from all other causes was 1:337, or 0.29 per cent, which compares with Körner's average figure of 1.05 per cent for all decades. Of course, in such a comparison the decrease in infant mortality, as well as the increase in longevity for the whole population, must be taken into account.

It is important to mention these facts inasmuch as sulfonamides are now so generally used at the

very onset of otitis media and in some clinics routinely, as well as preoperatively and postoperatively, that the student and the intern do not have a proper picture of otitis media as it existed prior to the introduction of chemotherapy.

Lindsay,³ in a review of recent progress in the treatment of acute otitis media, summarizes the present-day management. He states that the most effective time for chemotherapy is in the invasive stage. He prefers sulfadiazine, and urges that the initial doses should be gauged to obtain an early concentration in the blood of 6 to 10 mg. per 100 cc. This level should be maintained for two or three days, although the time to lower the concentration should be determined by the clinical condition. He states, nevertheless, that if certain indications are present before chemotherapy the best interest for the patient demands that surgery be carried out.

Hall and Spink⁴ advocate the use of sulfamerazine, and give the following directions for its administration. In adults and large children, 3 to 4 gm. is given as an initial dose, followed by 1 gm. every six hours until the temperature has been normal for forty-eight hours; then 0.5 to 1 gm. is given every eight hours and discontinued on the fifth to seventh afebrile day. In small children, 0.05 gm. per pound of body weight (the total not to exceed 4 gm.) is given initially, and treatment is continued with a dose of 0.05 gm. per pound of body weight in divided doses until the temperature is normal; then the dose is gradually reduced and is discontinued on the fifth to seventh afebrile day. In discussing the use of sulfamerazine it is stated that it is just as effective as sulfadiazine but requires smaller doses given less frequently and does not appear to be more toxic than sulfadiazine. The first point is important when it is desirable not to wake the patient for medication at night.

Ruskin⁵ advocates the addition of vitamin C to sulfonamide compounds, in the form of either sulfanilamide ascorbate or sulfathiazole ascorbate, in the treatment of chronic suppuration of a wound after mastoidectomy because of the known effect of vitamin C in hastening the healing of wounds.

Kolmer,⁶ in discussing the principles of treatment with sulfonamide compounds, says that the indiscriminate use of sulfonamide compounds is to be regretted because of the possibility and even the probability that the pathogenic bacteria will acquire resistance to the compounds. In using

*Instructor in laryngology, Harvard Medical School, associate surgeon, Massachusetts Eye and Ear Infirmary.

them for secondary bacterial infections of the common cold he quotes Spink,⁷ who states that chemotherapy should not be used in this group of infections except in patients with severe infections actually caused by hemolytic streptococci; in patients who are known to have cardiac defects, with the hope of being able to forestall bacterial endocarditis, and in obstetric patients who have contracted infection of the respiratory tract at or near term. Kolmer also asserts that treatment with sulfonamide compounds is not always a 'short cut to control of the disease, and he quotes Porter,⁸ who states that the otolaryngologist should not overlook prompt and adequate surgical measures, especially in cases in which there is pus to be drained or necrotic bone and infected thrombi to be removed. He believes that the use of sulfonamide compounds should be based on a bacteriologic diagnosis and gives the following list, in order of preference: staphylococcal infections, sulfathiazole and sulfadiazine; hemolytic streptococcus infections, sulfadiazine, sulfanilamide and azosulfamide; infections with *Streptococcus viridans*, sulfapyridine; pneumococcal infections, sulfadiazine; meningococcal infections, sulfadiazine and sulfanilamide; infections with Friedländer's bacillus, sulfadiazine and sulfapyridine; infections with *Pseudomonas pyocyaneus*, sulfanilamide and sulfathiazole; and infections with *Haemophilus influenzae*, sulfadiazine and sulfanilamide.

Much of the recent literature pertaining to the use of sulfonamides in otology is concerned with its use locally in surgical wounds. In a recent article Johnson and Spence⁹ record their experiences in 44 cases of acute mastoiditis in which the patients were treated by means of primary closure of the wound after filling the cavity with sulfonamide powder. They lay great stress on the necessity for a complete xenteration of the mastoid process. Great care should be taken to remove all infected cells. The perilyabyrinthine cells are removed until the horizontal semicircular canal is sharply defined. The zygomatic area is thoroughly cleaned out. In a number of cases the incus is brought into view. The mastoid cavity is then irrigated with normal saline solution, followed by thorough drying of the cavity and complete hemostasis. The cavity is then filled with sulfonamide powder. The wound is closed in two layers, more powder being dusted between the layers. In 12 cases in which one of the authors (L. F. J.) operated, there was complete healing of the postaural wound and resolution of the drum in twelve days. In another group of 8 cases operated on by various members of the hospital staff, the average postoperative stay was fourteen days. Twenty-five cases in which the mastoiditis had occurred secondary to scarlet fever had an average postoperative stay of twenty-eight days. A fourth group of 26 patients, used as a control, had an average stay of over fifty-two days, 24 of

these cases being secondary to scarlet fever. It should be noted that these authors advocate a thorough surgical technic, and it seems likely that incomplete surgery, more than anything else, prolongs the healing of mastoid wounds.

Livingston¹⁰ likewise recommends the use of sulfanilamide and sulfathiazole in postoperative mastoid cavities, but he states that in chronic cases sulfathiazole powder, although diminishing the odor and the purulent nature of the discharge, increases the discharge in quantity and that the caked powder often presents a problem. In cases of cholesteatoma the drug in no way alters the pathologic picture. Sulfonamide treatment hastens the healing in radical sinus surgery.

There is an increasing tendency to recognize the injurious effects of sulfonamide treatment. At the present time the serious effects of overdosage, such as agranulocytosis, severe anemia and renal damage, are well known. In otolaryngology there are other disadvantages. Because of the danger of sensitization nearly all authors now deprecate the use of sulfonamides for minor self-limited upper respiratory infections. It is true that during the present emergency civilians employed in essential war work have been under great pressure, particularly on the part of their employers, to remain at their work, even in the face of severe upper respiratory infection. Absenteeism has been so denounced that many people hesitate to report their illnesses. Among these the use of sulfonamide sprays, as well as the oral administration of these drugs, has been practiced.

Lessard¹¹ condemns the practice of those who have a tendency to give sulfonamides to patients at the slightest alarm, and cautions that should a later infection, such as meningitis or pneumonia, occur in a sensitized person, the use of sulfonamides would be impossible.

Livingston¹⁰ states that the problems that the otolaryngologist frequently encounters are as follows: previous inadequate administration; wrong choice of drug; infection refractory to sulfonamides; difficulty of differentiating an exacerbation of the infection and symptoms due to drug toxicity; and the masking effect of sulfonamides.

Leftwich,¹² recognizing the tendency of sulfonamide drugs to produce a hypersensitive reaction, states that most attempts to demonstrate sensitivity to sulfonamides by means of skin tests have failed. His studies were made on 76 patients at Johns Hopkins Hospital from March to July, 1943. The ability of the sulfonamides to combine with the plasma proteins suggested that, attached to the plasma proteins, they may act as haptens and in this way specifically sensitize the body. He writes:

Thinking along these lines it seems reasonable to suppose that there could be produced in the blood of the individual receiving a sulfonamide therapeutically, with an effective blood level, an antigenic substance capable

of causing sensitization in some instances, and possibly able to produce an allergic skin reaction when the serum of such an individual is injected intradermally in a person who is hypersensitive to the homologous sulfonamide. . . .

More than three hundred intradermal tests have been performed on the 76 patients studied, using forty different samples of serum as the testing agents. . . . These sera were obtained from patients suffering from some acute bacterial infection who had been treated with one or another of the drugs, whose blood cultures were negative and in whom the serologic test for syphilis was negative.

The serum was separated from the blood and placed in sterile rubber-stoppered containers, 0.5 cc. also being added to a culture medium, which was incubated for seventy-two hours as a check for sterility. The test was made by injecting intracutaneously into the flexor surface of the forearm 0.05 cc. of a control (normal) serum and 0.05 cc. each of serums from several of the patients treated with sulfonamides.

This test was found to be reliable in the diagnosis of drug sensitivity in 28 of 30 patients who had experienced definite drug reactions. It was positive in only 1 of 8 patients who were thought to be questionably sensitive clinically. In 26 patients in whom there was no evidence of sensitivity, the test was negative in 24. The 2 patients in this group who had positive tests had received sulfon-

amides for periods longer than six days so they may have been subclinically sensitized. Leftwich concludes that this method will show by a positive skin test whether or not a patient is sensitized to a specific sulfonamide, and also that this test is additional evidence that the drug sensitivity is an allergic reaction.

350 Dartmouth Street

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, October 4, 1944

A STATED meeting of the Council of the Massachusetts Medical Society was held in John Ware Hall, 8 Fenway, Boston, on Wednesday, October 4, 1944.

The meeting was called to order at 10:00 a.m. by the president, Dr. Elmer S. Bagnall, Essex North; 204 councilors were present (Appendix No. 1).

The Secretary presented the record of the meeting of the Council held on May 22, 1944, as published in the *New England Journal of Medicine*, issue of July 27, 1944.

Dr. John Homans, Suffolk, moved its acceptance and approval. This motion was seconded by Dr. Albert A. Hornor, Suffolk, and it was so ordered by vote of the Council.

REPORT OF THE EXECUTIVE COMMITTEE

The Secretary, in presenting the report of the Executive Committee (Appendix No. 2), said that the committee, in the name of the Massachusetts Medical Society, had endorsed the Fifth War Loan Drive and referred a telegram from Dr. Olin West, secretary of the American Medical Association, concerning it to the Committee on Finance.

He spoke of a question that had arisen in the committee as to the legality of the Council's action in adopting one of the recommendations contained in the report of the Committee on Medical Information Bureau. This recommendation had to do with an appropriation of \$2500, which was granted by the Council for the use of this committee. It was contended that the recommendation, calling for this appropriation, should have been first submitted to the Committee on Finance; failing in this, the Council should have made the appropriation contingent on its approval by this committee. The report went on to say that the committee instructed the President and Secretary to examine this situation. In the event that the appropriation had been improperly made, the President was urged to exercise his emergency powers so as to make this money available.

The report went on to say that the members of the committee were in receipt of an opinion on this matter written by the President which, in substance, stated that there was manifest evidence in the by-laws to the effect that it is the intention to have the Committee on Finance scrutinize any proposals for the expenditure of monies that are

extraordinary or other than routine. The Secretary added that the opinion also said that there is precedent for the appropriation of monies directly by the Council but that this has been contingent on the appropriation's approval by the Committee on Finance. The Secretary said that the President had exercised his emergency powers and that the money in question was available for the use of the Committee on Medical Information Bureau.

The report spoke of a request made by Mr. Powell M. Cabot, Massachusetts director of the War Manpower Commission. Mr. Cabot asked that the Massachusetts Medical Society set up machinery to aid his department similar to that set up to aid the Massachusetts director of the OPA. The report continued that this matter had been referred by the Executive Committee to the War Participation Committee, with instructions to co-operate with the Massachusetts director of the War Manpower Commission.

The report spoke of two communications that had been received on the same subject: one from the deputy surgeon general of the United States Army, Dr. George F. Lull, and the other from Lieutenant Colonel Mark C. Elworthy, chief of the Procurement Division. These communications concern a change in policy of the office of The Surgeon General whereby the Army is now commissioning certain graduates of Middlesex University School of Medicine. The conditions under which such commissions are granted are indicated in the body of the report.

The Secretary said that the committee had approved a plan submitted by the Red Cross for the training of volunteer nurse's aides in the treatment of infantile paralysis patients in the noncommunicable stage of the disease. He added that this matter had been submitted to the Committee on Public Health, which body had approved such action. He moved that the Council do likewise. This motion was seconded by Dr. David Cheever, Suffolk, and it was so ordered by vote of the Council.

Finally, the report said that the committee had reviewed the report of the Committee on Public Relations and had approved the recommendations contained therein, and certain *ad interim* appointments made by the President.

The Secretary moved the adoption of the report as a whole. This motion was seconded by Dr. Roy J. Heffernan, Norfolk, and it was so ordered by vote of the Council.

REPORTS OF STANDING COMMITTEES

Committee on Publications — Dr. Richard M. Smith, Suffolk, chairman.

No report.

Committee on Arrangements — Dr. Roy J. Heffernan, Norfolk, chairman.

The report, which was offered by Dr. Heffernan, is as follows:

The Committee on Arrangements, while recognizing the advisability of holding the annual meeting of the Society in various parts of the Commonwealth, believes that, owing to wartime restrictions on travel and to the limitations of hotel accommodations that may prevail next spring, it will be best to hold the 1945 annual meeting in Boston at the Statler Hotel.

It has also been thought advisable by your committee to increase the length of the meeting from two to two and a half days. To accomplish this the meeting will start on the afternoon of Tuesday, May 22, and continue through Wednesday and Thursday, May 23 and 24.

The annual meeting of the Council will be held Tuesday evening, May 22.

Dr. Heffernan moved the acceptance of the report. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council.

Committee on Ethics and Discipline — Dr. Ralph R. Stratton, Middlesex East, chairman.

No report.

Committee on Medical Education — Dr. Robert T. Monroe, Norfolk, chairman.

No report.

Committee on Membership — Dr. Harlan F. Newton, Suffolk, chairman.

No report.

Committee on Public Health — Dr. Roy J. Ward, Worcester, chairman.

The report, which was offered by Dr. Ward, is as follows:

The Committee on Public Health has had two meetings, both during the summer months. The committee is mindful of the contributions which the Society has made to public health in the past and hopes that further contributions can be made.

The first meeting was to explore the possibilities for concrete activities.

The second meeting discussed at length the proposed rheumatic-fever program of the Massachusetts Department of Public Health. The department is now rewriting the plan embodying recommendations of the committee, and it will be resubmitted to the committee later. The committee believes that the Department of Public Health earnestly desires the co-operation of the Society and is making every effort toward that end.

This is only a report of progress.

Dr. Ward moved the acceptance of this report. This motion was seconded by Dr. Guy L. Richardson, Essex North, and it was so ordered by vote of the Council.

Committee on Medical Defense — Dr. Arthur W. Allen, Suffolk, chairman.

No response.

Committee on Society Headquarters — Dr. J. Harper Blaisdell, Middlesex East, chairman.

Dr. Blaisdell, in offering this report, said that it contained no recommendation. He expressed the desire, however, to pass on to the Council certain information on and comments concerning the Society's headquarters. He added that the question of the site of such headquarters was a closed book.

for some time, a lease between the Society and the Boston Medical Library having been signed on October 1, 1943, to cover a period of five years. He said that this lease had been signed, on the part of the Society, by Dr. Roger I. Lee, at that time the president, and by Dr. William H. Robey, at that time the chairman of the Committee on Society Headquarters. By the terms of the lease, he continued, the Society pays the sum of \$6500 per year for the use of 3262 feet of floor space. It has the free use of John Ware Hall and one or two other halls including the banquet hall in the basement. He said that the rental was at the rate of \$2.00 per square foot. He expressed the thought that this was a generous rent.

He said that, during the summer, his committee had met with the Committee on Medical Information Bureau and that it had been proposed to set up the bureau in a space obtained by dividing up the present quarters of the President and Secretary. He added that, inasmuch as the Information Bureau was in the nature of an experiment and space elsewhere could be provided for it at the moment, it would be better to postpone any permanent partitioning. He said that this partition would cost at least \$800 and that this was another element influencing the committee's judgment.

He said that there was nothing on the outside of the building to indicate that therein was housed the headquarters of the Massachusetts Medical Society.

Finally, Dr. Blaisdell spoke of a meeting that the president, Dr. Elmer S. Bagnall, had arranged for that night with a gentleman who had just come into the service of the Massachusetts Dental Society and to which the Committee on Society Headquarters had been invited. He added that the gentleman in question is an expert on society headquarters, on publicity and on general relations between the professions, the press and the public.

The President announced that no vote on this report was necessary. He asked for a discussion of this report by way of questions or suggestions directed toward the committee. There was no response.

Committee on Finance — Dr. Francis C. Hall, Suffolk, chairman.
No response.

Committee on Industrial Health — Dr. Dwight O'Hara, Middlesex South, chairman.
No report.

REPORTS OF STATE-WIDE COMMITTEES

Committee on Legislation — Dr. Brainard F. Conley, Middlesex South, chairman.

Dr. Conley said that, inasmuch as last year was an off year in legislative matters, the committee had no report to offer.

Committee on Public Relations — Dr. Albert A. Hornor, Suffolk, secretary.

The report (Appendix No. 3) was offered by the secretary of the committee. The committee reported progress in two items: first, in the matter of better publicity for the Massachusetts Medical Society and, second, in regard to discussions held with the Massachusetts Division of Unemployment Security concerning sickness insurance for those employed in industry.

The report spoke of a discussion that had taken place between the members of the committee, representatives of the New England Roentgenological Society, the executive director of the Blue Cross, the administrator of the Waltham Hospital, the director of the Blue Cross and the president of the Massachusetts Hospital Association. This discussion concerned a proposed plan of the Blue Cross to include in the benefits offered under its contracts the sum of \$15.00 toward the costs of x-ray examination that the individual policyholder might require while hospitalized. In regard to this matter two recommendations were offered by the committee: first, that the Council should not approve, at present, the proposed plan of the Blue Cross to pay \$15.00 toward the costs of x-ray examinations in hospitals and, second, that discussion by the Massachusetts Hospital Service, Massachusetts Hospital Association, New England Roentgenological Society and the Committee of the Massachusetts Medical Society to Meet with the Massachusetts Hospital Association — Dr. Walter G. Phippen, chairman — should be continued.

Dr. Hornor moved the adoption of the first recommendation. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council.

Dr. Hornor moved the adoption of the second recommendation. This motion was seconded by Dr. Richardson, and it was so ordered by vote of the Council.

Dr. Hornor moved the acceptance and adoption of the report. This motion was seconded by Dr. Henry M. Landesman, Norfolk, and it was so ordered by vote of the Council.

The President at that point called on Dr. Charles E. Mongan, senior Massachusetts delegate to the House of Delegates of the American Medical Association, to report on the proceedings of the last meeting of that body (see Appendix No. 4).

Dr. Mongan concluded his report by saying:

Another member of our society has been called to the presidency of the American Medical Association. He is superbly equipped for the office, and well informed as to the nature of problems confronting organized medicine. He has served as member of the House of Delegates for ten years. He has been a member of the Board of Trustees for five years. He has been chairman of the Board of Trustees. He is a practicing physician, and has been president of the American College of Physicians.

extraordinary or other than routine. The Secretary added that the opinion also said that there is precedent for the appropriation of monies directly by the Council but that this has been contingent on the appropriation's approval by the Committee on Finance. The Secretary said that the President had exercised his emergency powers and that the money in question was available for the use of the Committee on Medical Information Bureau.

The report spoke of a request made by Mr. Powell M. Cabot, Massachusetts director of the War Manpower Commission. Mr. Cabot asked that the Massachusetts Medical Society set up machinery to aid his department similar to that set up to aid the Massachusetts director of the OPA. The report continued that this matter had been referred by the Executive Committee to the War Participation Committee, with instructions to co-operate with the Massachusetts director of the War Manpower Commission.

The report spoke of two communications that had been received on the same subject: one from the deputy surgeon general of the United States Army, Dr. George F. Lull, and the other from Lieutenant Colonel Mark C. Elworthy, chief of the Procurement Division. These communications concern a change in policy of the office of The Surgeon General whereby the Army is now commissioning certain graduates of Middlesex University School of Medicine. The conditions under which such commissions are granted are indicated in the body of the report.

The Secretary said that the committee had approved a plan submitted by the Red Cross for the training of volunteer nurse's aides in the treatment of infantile paralysis patients in the noncommunicable stage of the disease. He added that this matter had been submitted to the Committee on Public Health, which body had approved such action. He moved that the Council do likewise. This motion was seconded by Dr. David Cheever, Suffolk, and it was so ordered by vote of the Council.

Finally, the report said that the committee had reviewed the report of the Committee on Public Relations and had approved the recommendations contained therein, and certain ad interim appointments made by the President.

The Secretary moved the adoption of the report as a whole. This motion was seconded by Dr. Roy J. Heffernan, Norfolk, and it was so ordered by vote of the Council.

REPORTS OF STANDING COMMITTEES

Committee on Publications — Dr. Richard M. Smith, Suffolk, chairman.

No report.

Committee on Arrangements — Dr. Roy J. Heffernan, Norfolk, chairman.

The report, which was offered by Dr. Heffernan, is as follows:

The Committee on Arrangements, while recognizing the advisability of holding the annual meeting of the Society in various parts of the Commonwealth, believes that, owing to wartime restrictions on travel and to the limitations of hotel accommodations that may prevail next spring, it will be best to hold the 1945 annual meeting in Boston at the Statler Hotel.

It has also been thought advisable by your committee to increase the length of the meeting from two to two and a half days. To accomplish this the meeting will start on the afternoon of Tuesday, May 22, and continue through Wednesday and Thursday, May 23 and 24.

The annual meeting of the Council will be held Tuesday evening, May 22.

Dr. Heffernan moved the acceptance of the report. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council.

Committee on Ethics and Discipline — Dr. Ralph R. Stratton, Middlesex East, chairman.
No report.

Committee on Medical Education — Dr. Robert T. Monroe, Norfolk, chairman.
No report.

Committee on Membership — Dr. Harlan F. Newton, Suffolk, chairman.
No report.

Committee on Public Health — Dr. Roy J. Ward, Worcester, chairman.

The report, which was offered by Dr. Ward, is as follows:

The Committee on Public Health has had two meetings, both during the summer months. The committee is mindful of the contributions which the Society has made to public health in the past and hopes that further contributions can be made.

The first meeting was to explore the possibilities for concrete activities.

The second meeting discussed at length the proposed rheumatic-fever program of the Massachusetts Department of Public Health. The department is now rewriting the plan embodying recommendations of the committee, and it will be resubmitted to the committee later. The committee believes that the Department of Public Health earnestly desires the co-operation of the Society and is making every effort toward that end.

This is only a report of progress.

Dr. Ward moved the acceptance of this report. This motion was seconded by Dr. Guy L. Richardson, Essex North, and it was so ordered by vote of the Council.

Committee on Medical Defense — Dr. Arthur W. Allen, Suffolk, chairman.
No response.

Committee on Society Headquarters — Dr. J. Harper Blaisdell, Middlesex East, chairman.

Dr. Blaisdell, in offering this report, said that it contained no recommendation. He expressed the desire, however, to pass on to the Council certain information on and comments concerning the Society's headquarters. He added that the question of the site of such headquarters was a closed book

creased to cover marginal situations, although the usual reserve will be about 10 per cent.

This plan is open to all banks in Massachusetts, although it was started by the National Shawmut Bank. Some of the banks may adopt a different rate of reserve than others, and there may be a slight variation in the charge for this reserve.

This reserve, the 10 per cent having been taken out, is paid back to the doctor as payment on each account collected, unless the bank has some other charge against that particular physician, in which case the payment is credited against the other charge. As a result of the reserve feature, the term is shortened, so that the yield on the suggested rates compares closely with that of personal loans.

Whereas this has the appearance of collecting by the bank, it must be understood that the plan is in no way similar to the procedure of a collection agency. This plan is for current bills, not for the collection of bad bills. It is simply a method of making it easier for a man who eventually pays his bills to satisfy the legitimate claims of the physician, and to relieve the doctor of repeated monthly statements. It will take time for the plan to become the customary procedure. Over the years its use will expand.

Dr. George L. Schadt, Hampden, asked what was the basis on which the banks would consider a bill to be in the collection category. The President answered the question as follows:

The banks do not believe that it would be profitable for them if doctors took their bills that are five, six or seven years old, dumped them into a basket and gave them to the banks, but I am very sure that there would be no objection if some of these old accounts were turned over. Of course, the bank investigates the credit of each signer, and they will not accept the note unless they feel that there is a probability that the signer will go through. Furthermore the doctor, of course, should not endorse the note unless he thinks that his patient will probably stand behind it.

Dr. Schadt further inquired whether or not the doctor presents his bill to the bank on the completion of his work, whereupon it is paid by the bank, or whether he has to wait one, two or three months for such payment. Dr. Ellison replied that the arrangement can be made with the patient either during or after the illness.

Dr. Donald Munro, Suffolk, asked what the bank received. Dr. Ellison replied that, on amounts under \$100, the bank charges 50 cents a month.

Dr. Munro asked to whom the charge is directed. Dr. Ellison replied, "To the person who is being paid." He added that, if the doctor has a bill for \$100, he can deduct \$6, receiving \$94 in full payment from the bank. Dr. Munro replied that in essence this was a method whereby the doctor pays the bank to collect his bills. Dr. Ellison replied: "If the doctor wants to take out the charge, he is entitled to do so. If he does not, it is added to the amount of the face of the note, and the payee pays the bank's charges, plus the amount of the note."

Dr. Munro asked how this fitted in with the prospective plans of the Blue Shield. He added that he presumed that this plan did not apply to the income group that is affected by the Blue Shield. Dr. Ellison replied that the bank plan will supplement both the Blue Cross and the Blue Shield. He added that there are certain people to whom

the Blue Shield is not available and that the bank plan will serve such people.

In answer to further questioning on the part of Dr. Munro, Dr. Ellison reiterated his belief that the bank plan was complementary to the Blue Shield and not in competition with it.

Dr. Munro again emphasized the thought that, if the Society is going to play ball with a commercial organization that is obviously in the business for profit it should be clear whether or not the plan is in competition with the Blue Shield. At that point, the President observed that the plan has already been approved by the Council and that, therefore, this phase of the subject was not under discussion. Dr. Munro said that his purpose was to make clear to himself and to others certain phases of the subject that heretofore had been obscure.

Dr. George J. Connor, Essex North, asked what was the difference between this and the Morris Plan. Dr. Ellison replied that it was similar to the Morris Plan. Dr. Connor then observed that, if the doctor signs the note and the patient fails to come through, he, the doctor, is liable for the note. Dr. Ellison replied that this was the situation as he understood it.

Dr. Connor, in commenting on the statement coming from the bankers to the effect that most small loans were sought for medical purposes, said that, although such might be the reason given to the bankers by those seeking loans, the facts did not always bear this out. He spoke of two cases in his own experience wherein his bills were small and the loans sought from the Morris Plan were much more. In one instance the patient sought the additional money to finance a divorce, and in the other, to purchase an automobile.

At that point, the President said that the Massachusetts Dental Society was participating in this plan. He asked Dr. James C. McCann, president of the Massachusetts Medical Service, to discuss the relation between this plan and the Blue Shield. Dr. McCann replied as follows:

I am not qualified to do what you ask. There are certain impressions, however, that I might convey.

The first is that when the committee was working on a prepaid medical-care program, and when Dr. Bagnall was working on this program under the auspices of the Society, we were attempting to provide for the costs of medical care on a nonprofit basis. Yet we are faced with the fact that certain groups are approaching this problem on a profit basis. Whether commercial companies can accomplish more than we can remains to be seen.

There is unquestionably a call for an arrangement whereby those people who have seen fit not to participate in a prepayment program can accomplish this comfortable postpayment of their bills. Whether or not they participate is often up to the industry in which they work, and not up to themselves. This plan does offer them a way to handle it on a postpayment basis.

I might add that before Michigan undertook the prepayment program, they attempted a postpayment program, something of this character, on a nonprofit basis. It failed so definitely that they shifted to the prepayment basis.

The President at that point said:

Outside of the field of medicine he has been for many years one of the administrators of one of the largest universities in the United States. With such a record I think you will agree with me when I say that Dr. Roger I. Lee is eminently qualified to be the president of the American Medical Association.

The President asked Dr. Lee to stand so that all might see what he looked like. Dr. Lee arose and was greeted with loud applause.

Dr. Daniel B. Reardon, Norfolk South, asked the speaker if there is pending before Congress a bill establishing a public-health office in the Cabinet. Dr. Mongan replied in the affirmative. Dr. Reardon asked for the number of the bill. Dr. Mongan replied that he did not have the number at the moment but that he could get it. He added that the bill had been introduced by Representative Miller, of Nebraska, and that the latter is a doctor.

The President announced that Dr. Mongan's report called for no action.

Subcommittee Appointed to Meet With the Medical Advisory Committee of the Industrial Accident Board — Dr. Daniel J. Ellison, Middlesex North, chairman.

Dr. Ellison said that this subcommittee had no special report. He said that he had been appointed by Dr. Roger I. Lee, when the latter was president, a member of the general committee concerned with the conduct of the convention of the Associated Industrial Accident Boards and Commission of the United States and Canada. He added that this convention was held in Boston at the Statler Hotel in September, that it went off well and that he had enjoyed his part in it. He expressed his thanks to Dr. Lee for the assignment. (Dr. Ellison was chairman of the Reception Committee of the above event.)

Dr. Bagnall thanked Dr. Ellison for his report and called the Council's attention to an editorial and a communication from the Secretary's office that appeared in the *New England Journal of Medicine*, issue of September 28, 1944. He added that this material substantially reports the accomplishments of Dr. Ellison's committee. He urged the councilors to inform themselves on this matter.

He said that Mrs. Tousant had circularized the hospitals on the matter and that reprints of the editorial and the communication from the Secretary's Office will be sent to the chiefs-of-staff of all Massachusetts hospitals. He expressed the hope that the chiefs-of-staff will see to it that their respective members are informed with respect to these communications.

Subcommittee on Tax-Supported Medical Care — Dr. John J. Dumphy, Worcester, chairman.

The President announced that Dr. Dumphy was ill and that there would be no report from this subcommittee.

Subcommittee on Postpayment Medical Care (Bank Plan) — Dr. Daniel J. Ellison, Middlesex North, chairman.

In offering this report (Appendix No. 5), Dr. Ellison spoke as follows:

This report is presented without a meeting of the full committee having been held, and for this I sincerely apologize. Last August, Dr. Bagnall and I went to a meeting at the Parker House with a committee of the Massachusetts Bankers' Association, where Mr. McCarthy, vice-president of the National Shawmut Bank, presented this plan to the Massachusetts Bankers' Association. At that time he requested that nothing be said or done about the matter until he gave further notice of certain releases that he wanted to have made. The reason for that was that the outline or design of the brochures planned and the pamphlets and the wording of them was in process of being copyrighted, and he did not want some other organization to take this up through the publicity that might be given, and develop it prior to the receipt of the copyright. I have not heard from Mr. McCarthy, so I thought that it would be unwise to call doctors from all parts of the Commonwealth to a meeting where nothing definite could be accomplished. The meeting will, however, be held in the near future. I again apologize to the other members of the committee:

As you know, the spade work on this proposition has been ably done by our good president, Dr. Elmer S. Bagnall. The details of it have been presented at previous meetings. We are now concerned with the method of putting the plan into effect.

The original committee estimated that it would cost between \$500 and \$600 to put this over. Not one of us, and there were only three, had the courage to stand before the Council and ask for that sum of money. But it seems that miracles can happen, even for doctors. Mr. McCarthy got in touch with the American Bankers' Association, and was invited to meet with them in New York City, where they accepted this plan with open arms. They said that they would underwrite the entire expense of the publicity, and that they would design and draw up these brochures and pamphlets that are being passed around. So that the financial end of it is taken care of, not owing to the efforts of the committee, but to Mr. McCarthy's work.

Their plan is to start this proposition in Massachusetts. If it is successful, it will be developed in all other states of the Union. Payments will be made to the American Bankers' Association by the member banks of Massachusetts. Thus, the entire publicity will be under the care of the bankers. The doctors will be incidental in promoting this proposition.

The doctors will be visited in their offices or at such places as they wish by delegates appointed from the Association, and will be asked to join this plan. It will not be necessary for the doctors to go out among each other. However, your committee believes that it would be wise for the doctors in their district meetings to advertise the plan among each other.

The small-loans divisions of all banks in this state, as well as the small-loan companies, find that the second and third most frequent reasons given by people when applying for loans are for the payment of medical services. Obviously, a real need exists for this plan. Let it be understood that the rates charged for this plan are low, and easily explained. The charges are either added to or included in the doctor's fee.

There are two tables of rates. In the first, the charges connected with the loan are deducted, and in the second, the net plan, they are added to the note. A simple credit application is obtained, which the doctor or his secretary telephones to the bank. The facts are checked by the bank, and the doctor is notified when the note is approved. In due course the signed note is presented by the doctor to the bank for discount. To secure the doctor and the bank against loss, a reserve is set up for each account on the books at the bank in the doctor's name. The need for the reserve depends on the credit of the patient and on the doctor's practice. By agreement, the reserve may be in-

creased to cover marginal situations, although the usual reserve will be about 10 per cent.

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I might add that before Michigan undertook the prepayment program, they attempted a postpayment program, something of this character, on a nonprofit basis. It failed so definitely that they shifted to the prepayment basis.

The President at that point said:

I think that it must be apparent that a few of us have thought this thing through and have the right perspective on it. The committee, I am sure, will give further publicity to this matter. I understand that there is a plan in Springfield, initiated by the banks, that is operating very successfully. I have no direct information about that. There are also plans in other states, there being one in New Jersey and one in New York.

The head of the Advertising Department of the American Bankers' Association talked about this thing at the A.B.A. meeting a week or so ago, and he said that the bankers were very enthusiastic, and that they wanted the plan to be made nationwide. The Massachusetts program is a sort of pilot experiment, and the bankers think well enough of it so that they are willing to subsidize the plan.

A councilor asked who would be responsible in the event that a patient left an unpaid balance of 80 per cent. Dr. Ellison replied that the doctor would. He spoke of a man in his community who did a lot of work on venereal diseases. He added that it was the man's habit to have such patients obtain a loan from the Morris Plan Bank for \$50. Immediately on the failure of the patient to pay his regular installment to the bank, treatment was stopped. Dr. Ellison said that the doctor was driven to this by the fact that such people are notorious for not paying their bills.

Dr. Ellison moved the acceptance of the report. This motion was seconded by Dr. Richardson, and it was so ordered by vote of the Council.

(During the discussion of this matter, copies of a prospectus on the above matter had been passed among the councilors.)

Subcommittee Concerned with Prepayment Medical-Care Costs Insurance—Dr. James C. McCann, Worcester, chairman.

This report (Appendix No. 6) was offered by Dr. McCann. Dr. McCann moved that the Committee Concerned with Prepayment Medical-Care Costs Insurance, having completed its work, be discharged. This motion was seconded by Dr. Walter H. Pulsifer, Plymouth.

Dr. Allen G. Rice, Hampden, moved as an amendment that the original motion carry with it the thanks of the Council. This amendment being acceptable to the maker and seconder, it was declared by the President to be part of the original motion. It was so ordered by vote of the Council. (Dr. McCann was the recipient of loud applause as he left the platform.)

REPORTS OF SPECIAL COMMITTEES

Committee on Cancer—Dr. George A. Moore, Plymouth, chairman.

No report.

Committee on War Participation—Dr. Guy L. Richardson, Essex North, chairman.

Dr. Richardson reported as follows:

This year's work of the War Participation Committee had barely started when the report reached us of the death of Dr. William B. Breed, the first chairman of the com-

mittee. We had supposed his resignation had been sent in to lighten his efforts and to enable him to convalesce more quickly and that he would soon be back among us. Such was not to be the case, and our deliberations opened with the knowledge that the Council had lost a devoted and tireless worker.

It was apparent from the material Dr. Breed sent to me that he and his committee had done a prodigious amount of work. The records were carefully kept and catalogued and delivered to me in splendid shape.

So far as possible all projects undertaken or under discussion had been completed or decided. We were able to start afresh, and that was of particular help to Dr. Harold Giddings and myself, the two new members of the committee.

The first project that came to us was a request from the state office of the War Manpower Commission to assist them in drawing up a standard certificate form for a physician to sign whenever an applicant wished to change his job because of his health. The Commission thought that some doctors were too easily prevailed on by their patients to sign these certificates and that they were not careful to ascertain whether or not the old job really was detrimental to the applicant's health. Doctors too readily accepted their patients' statements about the health menace when the real reason for wanting to change jobs was to make more money or to work nearer home. As a result of this certificate abuse the work of the Commission in the war effort was being seriously interfered with. The following is an example of a case of apparent abuse: A dye worker presented a physician's certificate that his work was injurious to his health. Request to change employment was denied by the Commission. The worker then returned to the dye house and asked for his old job back. The employer refused because of the doctor's certificate stating that dye house work was injurious to that employee. The next day the worker returned with a statement from the same doctor to the effect that he had been completely cured and could safely resume his regular duties in the dye house.

The committee jumped into this project, believing it was what we were set up for. We advised a short certificate form and helped shorten it. If there is anything a physician hates to see pushed at him these days, it is a long questionnaire to answer and sign. We agreed to review the medical aspects of any doctor's certificate that the War Manpower Commission was uncertain about. Believing that the certificate abuse would be greatly lessened if doctors were fully informed of the harm caused by job jumping, space was given us in the August 3 issue of the *Journal* to depict the certificate form and to explain the whole matter.

It is gratifying here to reaffirm an earlier impression—that Massachusetts physicians will co-operate in any plan for the public good if the reason therefor is made plain to them. Thus far the committee has been asked to review not one of these new certificates. I should like to see that record maintained.

Let me quote from a letter to me under the date of September 18 and signed by Powell M. Cabot, state director of the War Manpower Commission: "In general, the opinion throughout the State is that this form has been of considerable value and has definitely corrected the situation which existed prior to its use."

The next appeal for aid came from the War Food Administration. Fats were scarce and were expected to become more so. Heavy cream prescriptions were being given out too freely by physicians. The purpose of the directive on heavy cream was thereby being defeated. The committee promptly assisted the War Food Administration to get the desired publicity. Through the local war-participation committees in all sections of the Commonwealth, we attempted to get full information to doctors and public as to the need for conservation of heavy cream, and to familiarize them with the opinions of the expert committees of the American Medical Association to the effect that heavy cream is rarely a necessity in medical treatment. We hoped this would lessen patients' applications for prescriptions and assist physicians in refusing to give them.

It has been estimated that the number of heavy-cream prescriptions coming in to the War Food Administration decreased more than 50 per cent after this publicity, and each succeeding week the decrease continues. The credit

for this remarkable showing belongs to Mr. John H. Sullivan, district supervisor of the War Food Administration, and his medical advisory committee, composed of some of our most respected physicians. They furnish the teeth for this act, and no amount of publicity in this instance is comparable to the effect of their decisions. It is a thankless job and gets them a lot of abuse. They are doing it with courage and fairness. I urge you to give them your support.

Another question brought before the War Participation Committee was the adequacy of hospital care for emergency cases in the largest cities of the Commonwealth — Boston, Springfield and Worcester. It was agreed that, in the smaller communities, no such problem existed. It was voted to send a letter to each of the major hospitals in those cities, asking how often in the last year it was necessary, for any reason, to refuse admission to an emergency case — either private or ward. These letters, forty-two in all, went out September 22, and already half the hospitals have replied. From a hasty reading of the answers, it appears that most of those hospitals never refuse admission of an emergency case. Some admitted having to turn away a few patients because of lack of beds or personnel. A complete report on this question will be made to the Council at a later date.

Dr. Richardson moved the acceptance of the report. This motion was seconded by Dr. Connor, and it was so ordered by vote of the Council.

Committee on Rehabilitation — Dr. William E. Browne, Suffolk, chairman.

Dr. Browne read into the record two letters. The first, which he had addressed to Dean A. Clark, Surgeon (R), United States Public Health Service, Physical Rehabilitation Section, Office of Vocational Rehabilitation, Washington, D. C., reads as follows:

Dear Dr. Clark:

I believe the date was April 26 of this year, I had the privilege as a member of the Boston Hospital Council of listening to your very worthwhile explanation of a program, not at that time completed, which had to do with rehabilitation.

You, no doubt, are well aware of some of the activities of the Massachusetts Medical Society. Perhaps when it was one hundred and fifty years old you read the late Harvey Cushing's paper concerning the Society and his paper was entitled "From Tallow Dip to Television." All during the years of its existence, as is the story with other state societies, its members have always tried to be of benefit and help to our citizens.

We have a committee of rehabilitation in the Massachusetts Medical Society. Pursuant to a communication from you dated February 5, 1944, our committee had a very pleasant dinner meeting with a representative of the Department of Rehabilitation of this Commonwealth acting under the direction of the Department of Education. Recently we received a query from the American Medical Association (a form query I assume), asking us what we had done and what we proposed to do in this matter of rehabilitation. Our reply was that twice since Wednesday, April 5, 1944, we had been in communication with the director of rehabilitation of the State, and each time had been informed, in substance, that committees in the various counties of the state were about to be set up, but up to now the Department of Rehabilitation in the state had not been ready to avail itself of any help which might be extended to it and which it really wanted from the physicians in the state and particularly the members of the Massachusetts Medical Society. On Monday, November 15, 1943, we communicated with the powers that be in Washington and asked whether or no it would be helpful to have two members from each of the district county medical societies in the state communicate with the Department of Rehabilitation for whatever assistance we might be in this matter of rehabilitation. We were informed that no definite program was at that time in operation.

Would you please consider this communication to you a personal one and in no sense going over the head of the director of rehabilitation in this state who is a very worth-

while individual. Busy though you may be, could you let our committee on rehabilitation know whether or not any state medical society in our country is at present functioning actively in any rehabilitation program approved by you and your department? Secondly, would you let me know if we are correct in assuming that we may not be of any service to the Department of Rehabilitation in our state or in the country as a whole until we are asked to be of assistance by those in charge of this program?

Sincerely yours,
William E. Browne

Dr. Clark's reply is as follows:

Dear Dr. Browne:

Thank you very much for your personal letter of August 30, which I found upon my return from a field trip.

The interest of the Rehabilitation Committee of the Massachusetts Medical Society in the expanded vocational rehabilitation program is very gratifying. There are a few facts about the development of this program which may be of interest to you.

You will recall that the Barden-LaFollette Act, Public Law 113 (78th Congress), was enacted by the Congress in July, 1943. The Office of Vocational Rehabilitation was established in the fall of last year and in January, 1944, the staff of the Physical Restoration Section was appointed by arrangement with the Surgeon General of the United States Public Health Service for the assignment of medical officers. The appointment of a national Professional Advisory Committee and the formulation of federal requirements and recommendations for physical restoration services in the state programs were the major activities of this section during the first portion of the year. These requirements and recommendations were considered at the meeting of the committee on March 3 and 4, 1944, and were issued as a section of the *Manual of Policies* to all state vocational rehabilitation agencies and state agencies for the blind on April 24, 1944.

The physical restoration aspects of the program constitute an entirely new activity for almost all the states and require considerable interpretation and assistance to state officials by the regional representatives and technical consultants of this office. The first installment of the physical restoration amendments to state plans, dealing with the administrative organization and qualifications for administrative personnel for the physical restoration unit, was due in this office on July 1, 1944. The second installment of the physical restoration amendments to state plans, dealing with the general criteria to be followed in the provision of physical restoration services, medical diagnosis, scope of physical restoration services, standards for physicians and other professional personnel, and rates of payment to hospitals will be due in this office on January 1, 1945. The complete operation of the physical restoration phases of the vocational rehabilitation program probably will be in effect in most states by July 1, 1945.

In the light of these facts, the inauguration of physical restoration services by state agencies will require some additional time before the necessary administrative staffs are recruited and policies established. In order to qualify for federal grants-in-aid the state agencies are urged to secure competent technical advice through advisory committees. It is recommended by the federal office that such committees be appointed by the state agencies after consultation with appropriate professional groups and that they include physicians representing the principal specialties of medicine concerned with rehabilitation and representatives of public health, hospital administration, nursing, medical social work, physical therapy and occupational therapy. The medical specialties particularly stressed are orthopedics, tuberculosis, psychiatry, ophthalmology, otology and so forth. On the basis of information thus far received practically all state medical societies have indicated their willingness to co-operate and in many instances have suggested physicians for the state professional advisory committees. I am sure the officials of the Massachusetts rehabilitation agencies are looking forward to the valuable assistance which can be rendered by your committee in conducting the physical restoration program, and I am, therefore, sending copies of this letter to Mr. Irwin Ristine, regional representative, Mr. Herbert A. Dallas, director, Division of Vocational Rehabilitation for Massachusetts,

and Mr. Arthur Sullivan, director, Massachusetts Division for the Blind.

I hope that I shall have an opportunity of discussing the rehabilitation program with you at some future date during a visit to Massachusetts.

Very truly yours,

DEAN A. CLARK, Surgeon (R), U.S.P.H.S.

Dr. Browne moved that the Council approve this correspondence. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council.

Dr. Browne endeavored to impress the Council with the importance of keeping up to date on this matter, saying that some day this is going to be a big problem and that he did not want it said at some future time that the Government had tried to get medical societies to do the right thing and finally had to do it itself.

Dr. Browne moved that his report be accepted as a report of progress. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council.

Committee on Postwar Loan Fund—Dr. George Leonard Schadt, Hampden, chairman.

Dr. Schadt spoke as follows:

The committee has no formal report at this time. It is merely a brief informal report to say that the committee, through its various members, is appearing before the different districts during the next month or two, and then early in November we will get the questionnaire out suggested by the Council at its last meeting. We hope that every member will return that questionnaire postcard promptly so that we may know how the Society as a whole feels on this plan.

The President expressed the thought that no action by the Council on the report was necessary.

Military Postgraduate Committee—Dr. W. Richard Ohler, Norfolk, chairman.

Dr. Ohler reported as follows:

This will be a very brief report. Since the annual meeting the work of the committee has progressed as usual, with no letup during the summer months. Since October, 1943, when the Massachusetts Medical Society committee joined forces with representatives from other state societies in New England, and with representatives from the American Medical Association, the College of Physicians and the College of Surgeons, to organize what is now known as the New England Committee for War-time Graduate Medical Meetings, two hundred and nine such meetings have been given in twenty-one Army, Navy and Coast Guard installations in the New England area by a group of one hundred and sixty-nine instructors.

As a mark of appreciation for the work done by the various instructors, the First Naval District tendered a dinner to all instructors throughout New England at the Chelsea Naval Hospital on September 25. Needless to state, the occasion was very much appreciated by all who have given of their time to make this program a success.

Since our last report, this committee has lost the services of Dr. William B. Breed. In this particular effort, as in any work or endeavor in which Dr. Breed had a part, we miss his wise counsel, his enthusiastic support and, beyond all else, his great friendliness and human understanding.

Dr. Ohler moved the acceptance of the report. This motion was seconded by Dr. Merrill C. Sos-

man, Suffolk, and it was so ordered by vote of the Council.

Medical Advisory Committee to Regional OPA—Dr. Joseph Garland, Suffolk, chairman.

Dr. Garland reported as follows:

The problem of determining extra ration allotments on certificates of patients' necessity continues to be a vexing one. Point values shift frequently and difficulties are often encountered in obtaining unrationed foods. Thus, with the individual still receiving $7\frac{1}{2}$ red points weekly, the point value of butter has jumped to 20 points per pound, and, although many types of meat are off the ration list, they cannot always be found on the counters, although in this respect it is worth mentioning that only 29 per cent of all the meat in the country at this time is rationed. Many persons, moreover, are still apparently unable or unwilling to adjust themselves to the use of fats and meats of low or no point value.

To these facts, and to the new regulation that local boards are allowed to issue extra points for diabetes and active tuberculosis only, may be attributed the increased rate at which applications are coming to the regional office—815 in the first twenty days of September. It seems apparent to the committee that many more certificates are being submitted than is justified on the basis of the facts in individual cases, which again brings up the problem of publicity and education for both the public and physicians. As the need for food rationing continues, and there seems to be no immediate prospect of its coming to an end, this education should be brought about by an increased reliance on local advisory committees—perhaps in most instances the local war-participation committees already in existence. Committees have been formed this summer in Scituate and Brockton, and others are scheduled for Lawrence, New Bedford, Springfield, Worcester and Pittsfield. The policy will be extended as the need arises.

Advisory committees are now functioning in Connecticut, New Hampshire and Maine, in addition to Rhode Island, which has helped somewhat in lightening the labors of the Massachusetts committee.

When new restrictions on the prescription of heavy cream were imposed on August 1, this committee was incorporated into a new and larger advisory committee to aid the War Food Administration.

Dr. Garland moved the acceptance of the report as one of progress. This motion was seconded by Dr. Richardson, and it was so ordered by vote of the Council.

The President solicited the support of the sub-committees that have or will be appointed under this program. He added that it was important to demonstrate the Society's capacity and willingness to participate in these emergency matters to the end that we may not later be criticized for holding out against or opposing any of the governmental program.

Committee on Medical Information Bureau—Dr. Walter G. Phippen, Essex South, chairman.

Dr. Phippen reported as follows:

This is simply a report of progress. The telephone has been installed in the room across the corridor from Dr. Tighe's office. We are in process of hiring an operator. We are holding a meeting on Wednesday afternoon, October 25, at 4:00 p.m., to which are invited representatives of all the hospitals in Greater Boston to discuss the technical operation of the Bureau, and we hope to have it in operation soon. It will be listed in the telephone directory under Massachusetts Medical Society, Clinical Information. Unfortunately the telephone company allows only two words so the word "Bureau" must be eliminated.

Dr. Phippen moved that the report be accepted as one of progress. This motion was seconded by Dr. Cheever, and it was so ordered by vote of the Council.

Committee on Postgraduate Instruction — Dr. W. Richard Ohler, Norfolk, chairman.

No report.

Committee on Physical Therapy — Dr. Arthur L. Watkins, Middlesex South, chairman.

The report, which was offered by Dr. Watkins, is as follows:

This committee has functioned chiefly with the aim of increasing the use of physical therapy by general practitioners. To accomplish this purpose a paper discussing physical therapy in general practice has been published in the *Journal* and monthly symposiums have been given in service hospitals in connection with the wartime graduate medical meetings.

Dr. Watkins moved the acceptance of the report as one of progress. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council.

Committee on Expert Testimony — Dr. Frank R. Ober, Suffolk, chairman.

This report (Appendix No. 7) was offered by Dr. Ober.

Dr. Ober moved the acceptance of the report. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council.

Dr. Ober moved the adoption of the following recommendations contained in the report:

1. That a standing committee of five or more, to be called the Committee on Medicolegal Problems, be appointed by the president.
2. That the by-laws of the Massachusetts Medical Society be amended to provide for such a body.

This motion was seconded by Dr. Schadt.

Dr. Rice expressed the wish to hear some debate concerning the necessity of establishing another standing committee. He added that the Committee on Ethics and Discipline had had only two such cases and that this committee is not overburdened.

Dr. Reginald Fitz asked if these recommendations did not imply a change in the by-laws and, if that was so, if some special action was not required.

The President replied that such was embodied in the second recommendation.

Dr. Carl Bearse, Norfolk, said that the matter of creating a standing committee deserved serious consideration. He added that questions concerning medical expert testimony are now being taken up by many other state medical societies. He stated that Michigan and Connecticut are working on a plan at the present time and that California has a plan, which goes in for education along these lines, there being a panel of physicians who talk to lawyers on the medical aspect of expert testimony. He said that he had noted recently that there were 4000

malpractice suits in the country each year. He added that this problem was coming up constantly and that it was his opinion that the problem could best be met by the creation of a standing committee.

Dr. Hornor asked:

Is it the intention that this committee will serve to offer a panel, or the equivalent of a panel, to judges so that the judges will know whether the man who is testifying, be he a neurologist, laryngologist or orthopedist, really knows something about his specialty? It seems to me that what we need is prevention of poor testimony rather than the disciplining of people who have testified poorly.

I think that we need to help the judges and the courts to know whom they want to testify before them. And if that would be a part of the work of this committee, I should be much in favor of it.

Dr. Ober, in reply to Dr. Hornor, said that his committee did not consider that it was its function to discuss how this should be done. He continued as follows:

We thought that that should be left to a standing committee, and that that standing committee should not proceed overnight to try to reform the whole procedure of expert testimony. Your scheme, however, is a part of it.

Now there may be some objection to the panel system, and perhaps we should not get into an argument about that now. That should come up as a report of the standing committee. We hope to submit a by-law that will cover the duties of the standing committee, and that by-law should be discussed when presented. I do not believe that this is the day to present the by-law. This committee should be instructed to present a by-law on the functions of such a standing committee, similar to the by-laws that describe the functions of other standing committees.

There are a great many matters that have to be considered in this thing. First, there is the bad medical witness, and there is the court testifier who goes around testifying as an expert in all sorts of things. There is the question of rules of procedure in the courts, and the question of subpoenas, having a constable come into your office and serve you with a subpoena as an ordinary witness, and you get down there to the court and find you are going to be qualified as an expert witness, and that does not seem to be quite fair to some of us. Then there is the question of one doctor testifying against another. So there are a great many aspects of this thing that cannot be settled by the Committee on Ethics and Discipline.

The Committee on Ethics and Discipline is a court, as I see it, to settle many problems of this nature. The Committee on Medical Defense, of which Dr. Allen is chairman, has, of course, headed off a great many suits for malpractice, but we believe, in addition, that there is an educational aspect. Every doctor should be informed concerning what constitutes malpractice and concerning proper conduct toward his patient, so that he does not interfere with the code of ethics of the American Medical Association and the code that we have adopted and so that he will not tell some patient, "Well, so-and-so just treated you rottenly." We should like to stop all that.

We believe that such a committee has a special job to do, and that this legal thing is in its infancy. It has not been changed in the last five hundred years, and with a standing committee that has a constant function, — and the standing committee should be changed so that new blood would be instilled into it every so often, — we think that the Society would get farther in straightening out some of the bad expert testimony that is going on.

The Briggs Law has done a tremendous amount of good to straighten out testimony in criminal cases in which the problem of insanity arises, and it has cut out a lot of poor expert testimony. Some of you, perhaps many of you, will remember what happened in the Thaw case a great many years ago. We do not have that in Massachusetts.

Dr. Schadt spoke as a former chairman of the special committee. In replying to Dr. Hornor's

question, he said that he and his committee had in mind the question of setting up a panel at that time. He said that he had discussed this with certain representatives of the Massachusetts Bar Association and that they were sympathetic. He added that the importance of this committee is great and that a committee of this kind could do great work.

Dr. Munro spoke as follows:

There is no question but that this is a tremendously important problem. I should like to emphasize what Dr. Horner has said and what Dr. Schadt has said, and what Dr. Ober has also emphasized. This problem is so intimately bound up with the law of testimony and the power of the courts to declare a man expert or not expert on what seems to the medical profession to be inadequate evidence, that I think that the Society should consider very carefully the advisability of obtaining active co-operation from the Massachusetts Bar Association before committing itself to the creation of a standing committee.

Now I do not mean that a standing committee should not be created. I think a standing committee should eventually be created, just as Dr. Ober suggests, but to create a standing committee means that certain rules, procedures and duties must be outlined, also as he requests.

It does not seem wise to me for the Society to go off the deep end at this moment, and create such an important committee, until it knows very well what the rules and procedures and functions of that committee are going to be, and those cannot be known, I believe, until the active co-operation of the Massachusetts Bar Association is obtained.

I should think that it would be very much more to the purpose to have this thing handled during this formative period by the special committee, and then when all organizations and the Massachusetts Bar Association have co-operated, as I am sure they will, a standing committee could be formed with rules and duties and methods of procedure that would fit the case as it actually exists, and not as it was thought to exist.

Dr. Charles C. Lund, Suffolk, spoke as follows:

The question before the house is whether or not we should create a standing committee.

It seems to me that Dr. Ober's report has not given us quite enough information to make a decision at this time. To decide whether we should have a permanent committee rather than a temporary one, I think we should know from Dr. Ober, first, what he has done, second, what his problems are and, third, why those problems cannot be solved by the present committee. I probably should be in favor of a standing committee because I know that this subject is important and because I want to see everything done by the Society that can be done to keep medical testimony on the highest plane.

Dr. Cheever arose to say that he thought he might clarify some of the issues. He spoke as follows:

Almost everything that has been said was brought up in our committee, and we considered it very carefully, and our committee is not at all convinced or sure of how much we can accomplish.

Now there are a number of interesting things to remember. Obviously, there are three major parties to this situation. There is the judiciary; there are the lawyers; and there are the doctors. The judiciary, of course, constitutes the entire organization of the courts. You will be perhaps rather surprised to know that there are ten thousand practicing lawyers in the state but that only fifteen hundred of them belong to the Massachusetts Bar Association. Only two thousand of them belong to the Boston Bar Association. It is perfectly evident, then, that eight thousand of the ten thousand practicing lawyers in Massachusetts are outside the jurisdiction of any agreement that those two bar associations might make. That is a very unfortunate situation.

Dr. Horner's question about the panel was something that we considered carefully and thought that we could not possibly decide. It seems to me almost impossible that a panel of the members of the Massachusetts Medical Society could be arranged and constituted and accepted by the judiciary and accepted by the lawyers in connection with these cases.

We consulted with the secretaries of the bar associations and learned an interesting fact: there is a movement on foot to integrate both these bar associations and all the lawyers in the state into a single association. And if that can be done, it is obvious, I should suppose, that their rulings and decisions would have to be observed by all the lawyers of the Commonwealth. When that is done, we could proceed with more certainty of some success.

There is another thing that I should like to emphasize in connection with what Dr. Rice said, and that is that it would seem, having read a little editorial note in the *Journal* some weeks ago, as though it were not generally known how adequately the Committee on Ethics and Discipline in the past has handled this situation.

We have always had—I can personally testify for twenty years—a Committee on Ethics and Discipline that has been glad to receive complaints about unimpaired medical expert testimony, that has considered those cases and that, in a good many instances, has disciplined the offender even to the extent of securing his resignation from the Society. So that if you will read the statement about the Minnesota Bar Association, you will find that what they are congratulating themselves about is an arrangement precisely similar to that, so far as I can see, that has always obtained here. So we are not so very far behind.

It did seem to this committee, of which I am a member, that the Society as a whole is sufficiently informed about the functioning of the Committee on Ethics and Discipline in these cases. Of course, we can inform it, but it seemed to us that the creation of a new standing committee would serve as a means of so informing the Society, and bringing the matter more acutely into the foreground. And it was our belief and intention that this new committee would organize the work, would sift the cases as the evidence was presented, and present to the Committee on Ethics and Discipline for final adjudication the issues involving the question of disciplining an offender. That is about as far as we were able to go.

Dr. Browne observed that the litigant in dealing with the subject must not be forgotten, for without him there would be no case. He thought it would be questionable whether or not a panel would work out. He said that it was discretionary with the judge whether or not the individual doctor could qualify as an expert. He added that judges exercise this discretionary power in various ways. Dr. Browne expressed himself as feeling that it might be wise to refer this matter to the Executive Committee. Reverting to the matter of a panel, he thought such might be a valuable thing if one of the panel were to listen to medical testimony offered in court. He finally concluded with the thought that he was quite sure that a standing committee will ultimately be a necessary and helpful thing for the Society. He questioned, however, the wisdom of doing this without further deliberation.

Dr. Schadt was recognized by the chair. He referred to the remarks made by Dr. Rice and said that the work of this committee should be to educate doctors, both members and nonmembers of the Society, so that they may become good witnesses to the end that they may never have cause to appear before the Committee on Ethics and Discipline. He concluded by saying that he thought

that this would be a valuable committee for the society.

Dr. Stratton expressed himself as favoring such committee, particularly its educational function. He did not, however, think that a standing committee should be created until such time as the special committee brought into the Council a definite program with which the Massachusetts Bar Association concurs. He added that, when and if such a situation was realized, the Committee on Ethics and Discipline would be relieved of a tremendous amount of work usually associated with assembling the facts in any given case.

Dr. Ober expressed the thought that the Society was not going to get anything out of the lawyers until it had done something itself. He spoke as follows:

Under the prevailing system of trial by jury or before a judge the conduct of a lawsuit is a bilateral contest to see which side will win. In the procedure of producing direct testimony, everything favorable to the client is presented, and on cross-examination everything may be done to discredit or destroy that testimony. Too often the debate is emotionalized and dramatized by one side or the other, in order to influence the jury. Therefore, it would seem in the interests of justice that some other method of considering expert testimony might be worked out which would be superior to our present system.

He concluded that this would be one of the main functions of this standing committee.

At that point the recommendations of the committee were restated. Then, they were adopted by a standing vote of the Council.

The Secretary arose to say that the adoption of the recommendations did not constitute a formal amendment to the by-laws and that, if such an amendment were to be acted on at the annual meeting in 1945, it must be offered at this meeting or at the meeting in February.

The President asked if anyone was prepared to introduce a formal amendment.

Dr. Bearse moved that Chapter VII of the by-laws be amended by adding Section 16, to read as follows:

The Committee on Medicolegal Problems shall consist of five fellows. It may appoint auxiliary members. It shall concern itself with medicolegal problems.

This motion was seconded by Dr. Lester M. Felton, Worcester.

Dr. William A. R. Chapin, Hampden, moved that this matter be laid on the table. He said that he had made this motion because he thought standing committees were something to think about and because he did not believe that amendments to the by-laws were done orderly when devised in two minutes. Dr. Chapin's motion was seconded by Dr. Munro, and it was so ordered by vote of the Council.

Committee on Automobile Insurance Claims — Dr. Henry C. Marble, Suffolk, chairman.

In connection with the above committee, the President made the following statement:

The question arises whether or not to continue this committee. The committee has made no report, and it is the opinion of the President and the Secretary that a committee that makes no reports should not be carried on the rolls year after year. If there is no objection from the Council, this committee will be declared discharged, with thanks, because they did a good piece of work in organizing a plan for the direct payment to physicians by a gentleman's agreement with the insurance companies.

Do I hear any objection?

There was no response.

Committee to Study the Practice of Medicine by Unregistered Persons — Dr. Richard Dutton, Middlesex East, chairman.

Dr. Dutton said his committee had no report. He moved that the committee be discharged; the President added "with thanks," he being mindful of the applause with which this committee's report had been received several years previously. This motion was seconded by Dr. Conley, and it was so ordered by vote of the Council.

Committee to Meet with the Massachusetts Hospital Association — Dr. Walter G. Phippen, Essex South, chairman.

No report.

Committee on Maternal Welfare — Dr. Raymond S. Titus, Norfolk, chairman.

No report.

APPOINTMENTS

The President made the following nominations:

Auditing Committee:

Dr. Z. William Colson, Essex North, chairman.
Dr. David G. Cogan, Middlesex South.

To the Council:

Dr. Matthew J. Bachulus, Hampden, replacing Dr. Edward A. Knowlton, resigned.
Dr. Joseph A. Daley, Middlesex South, replacing Dr. John J. Cochran, deceased.
Dr. Kenneth J. Tillotson, Middlesex South, replacing Dr. Sumner H. Remick, a member *ex officio*.
Dr. Abraham Myerson, Norfolk, replacing Dr. Roy J. Heffernan, a member *ex officio*.
Dr. James J. Regan, Suffolk, replacing Dr. Reginald Fitz, a member *ex officio*.
Dr. John Homans, Suffolk (this district was entitled to one more councilor).
Dr. Theodore L. Story, Worcester, replacing Dr. Roy J. Ward, a member *ex officio*.
Dr. W. Richard Ohler, Norfolk, replacing Dr. Edward L. Kickham, deceased.

To the Committee on Public Health:

Dr. Conrad Wesselhoeft, replacing Dr. Roger I. Lee, resigned.

To the Committee on Postgraduate Instruction:

Dr. W. Richard Ohler, replacing Dr. Reginald Fitz as chairman.

To the Committee on Maternal Welfare:

Dr. Raymond S. Titus, chairman, replacing Dr. Louis E. Phaneuf, resigned.
Dr. Benjamin deF. Lambert.
Dr. Ralph E. Cole.

To the Committee on Postpayment Medical Care:

Dr. Daniel B. Reardon, replacing Dr. Walter L. Sargent, resigned.

To the Medical Advisory Committee to Regional OPA:

Dr. Loring Grimes.

To the Committee on Nominations:

Dr. Harry F. Byrnes, alternate member from Hampden District, replacing Dr. Edward A. Knowlton, resigned.

To the Board of Censors, Norfolk District:

Dr. H. Allan Novack, replacing Dr. Saul Berman, deceased.

Representative to the Massachusetts Central Health Council:

Dr. James W. Bunce, Berkshire, replacing Dr. Robert J. Carpenter, resigned.

Voting Member in Massachusetts Hospital Service, Incorporated:

Dr. Albert A. Hornor, replacing Dr. William B. Breed, deceased.

Representative on the Massachusetts Nursing Council for War Service:

Dr. David D. Scannell.

The President asked if there were any nominations from the floor. There being no response, Dr. Chapin moved the approval of the nominations. This motion was seconded by Dr. John B. Hall, Norfolk, and it was so ordered by vote of the Council.

NEW BUSINESS

The President read the obituaries of three former councilors.

DR. WILLIAM B. BREED, of Newton, died August 21, 1944. He was in his fifty-second year.

Dr. Breed received his degree from Harvard Medical School in 1920. He had been a member of the Council since June, 1929, and nominating councilor since 1939. At the time of his death he was a member of the Committee on Publications, having been appointed to that committee in February, 1940, and a voting member in Massachusetts Hospital Service, Incorporated. He was a member of the Board of Censors of Suffolk District from 1933 to 1937 and was supervising censor from 1937 to 1938. He was formerly chairman of the Committee on War Participation and a member of the Committee on Prepayment Medical-Care Costs Insurance and the Committee on Legislation. He was associate editor of the *Journal* from 1923 to 1937 and a member of its editorial staff from 1937 to 1942.

He had been secretary-treasurer of the National Committee for Wartime Graduate Medical Meetings since its organization in the summer of 1943.

Dr. Breed was a staff member at the Massachusetts General Hospital and an associate in medicine at Harvard Medical School. He was also a member of the American Medical Association, the American College of Physicians, the New England Heart Association and the American Clinical and Climatological Society.

His widow and three children survive.

DR. EDWARD L. KICKHAM, of Brookline, died August 10, 1944. He was in his forty-ninth year.

Dr. Kickham received his degree from Tufts College Medical School in 1923. He has been a member of the Council since 1937 and, at the time of his death, was a member of the Massachusetts Committee of the Procurement and Assignment Service. He was a member of the Board of Censors of Norfolk District from 1936 to 1939 and was supervising censor from 1939 to 1940.

He was a member of the obstetric and gynecologic staffs of the Carney Hospital and St. Elizabeth's Hospital, having been associated with the former since 1924 and with the latter since 1930. He had been instructor in gynecology at Tufts College Medical School since 1930.

Dr. Kickham was a fellow of the American College of Surgeons and the New England Obstetrical and Gynecological Society and a member of the American Medical Association, the American Board of Obstetrics and Gynecology and the Boston Obstetrical Society. He was treasurer of St. Luke's Guild of Boston.

His widow, two brothers and a sister survive.

DR. CHARLES A. SPARROW, of Worcester, died September 20, 1944. He was in his sixty-first year.

Dr. Sparrow was born in Marion and graduated from Amherst College in 1906, receiving his degree from Harvard Medical School in 1909. He had been a member of the Council since 1938. He was a member of the Committee on Public Relations from 1939 to 1943. He was an associate editor of the *Worcester Medical News*, a publication of the Worcester District Medical Society, as well as a past president of that society.

He was appointed to the staff of the Memorial Hospital in 1916 and in 1925 became head of the Pediatric Clinic there.

Dr. Sparrow perfected, as chief of the Medical Division of the Massachusetts Committee on Public Safety in Worcester, arrangements for the work of doctors, nurses and ambulances in case of enemy air activity.

He was a member of the American Academy of Pediatrics and of the New England Pediatric Society.

His widow, a son, a daughter and a sister survive.

The President asked the councilors to stand for one minute in silent tribute to these men.

The Secretary read the following excerpt from Chapter V, Section 1, of the by-laws:

The censors of the several district societies shall meet for the examination of applicants semiannually on the first Thursday in May and on the first Thursday in December.

He referred to the Council a membership certificate that had come from a district medical society in which the censors' examination had been held on October 6, 1943. He spoke of having written the district society and of having received a reply to the effect that the doctors in the district were extremely busy. Dr. William D. Kinney, Barnstable, said that he had been present at the May meeting when this examination had been started and that, owing to an emergency, the examination had to be discontinued and was not completed until October. Dr. Kinney moved that this candidate be admitted to the privileges of membership in the Massachusetts Medical Society. This motion was seconded by Dr. Henry W. Godfrey, Middlesex South, who expressed it as his feeling that this candidate, having started his examination at the proper time, should be admitted as of that date. It was so ordered by vote of the Council.

Dr. Allen G. Rice, Hampden, asked who sets the hour of the Council meetings. The President referred this question to the Secretary, who replied that the Council itself sets the hour of its meetings.

Dr. Rice pointed out how difficult it was for councilors from Springfield and points farther west to arrive on time for a 10:00 o'clock meeting. He said that, as it is now, such councilors must leave Pittsfield around 5:00 o'clock in the morning and Springfield at 6:45. He added that, if the hour of meeting were changed to 10:30 a.m., councilors could leave Springfield at 8:00 a.m. and arrive at the meeting on time. Dr. Rice made a motion to

that effect. This motion was seconded by Dr. William Dameshek, Norfolk, and it was so ordered by vote of the Council.

Dr. Dameshek moved that the Council set up a committee for the consideration of transfusions and blood grouping. This motion was seconded by Dr. Hornor.

In support of this motion, Dr. Dameshek spoke as follows:

I think all of us will agree that transfusions and blood grouping technics have come to the foreground a great deal in recent years. Furthermore, there has been the great expansion of blood banking, the Rh factor has been discovered and so forth. The number of transfusions has increased, and a great many reactions, sometimes fatal, have occurred. I happen to have seen a number of them in the past several years in the various parts of the Commonwealth. So I am beginning to believe more and more that there should be a committee of the Society to consider transfusions, standardization of the methods, the training of technical help doing the transfusions, the various agglutination tests, the Rh factor, transfusion reactions and so forth. This committee could gather information, it seems to me, of great importance to the members of the Massachusetts Medical Society, and could perhaps standardize procedures in various hospitals. I think that it is important for the Massachusetts Medical Society to do this first, before the Massachusetts Department of Public Health takes it over.

He said that it was his idea that this committee should be appointed by the President and that he was willing to leave the number of members to serve on it to the same authority.

Dr. Schadt asked whether such a committee would set up rules and regulations for community hospitals, private hospitals, private laboratories and physicians. Dr. Dameshek said that he was in the process of writing a letter to the editor of the *Journal* and that he would take up Dr. Schadt's question in that letter. He added, however, that he did not have it in mind that this committee should supervise the business of transfusions in hospitals and laboratories but rather that it should gather material and data on this subject and disseminate the information so obtained.

He went on to say that a great many blood groupings have been done with faulty serum, that a great many blood groupings are being done by incompetent personnel, that there are a great many reactions due to incompatibility that has not been properly checked, that the patient has not been watched properly during the administration of the first 50 to 100 cc., that too many transfusions of whole blood are now being given, that at times the typing and cross-matching procedures are not properly checked and that whole blood is frequently given while the patient is under a general or spinal anesthetic, the patient under such circumstances not having the full possession of his senses or his sensibilities. He expressed the thought that the standardization of the whole procedure might well be a function of the committee.

Dr. Lund said that he did not see how this committee could be of particular benefit or why a com-

mittee should be set up in this and not in other fields. He concluded by saying that it seemed to him that the answer to Dr. Dameshek's problem was for him to do a little study, write a paper and publish it in the *Journal*.

Dr. Hornor said that, when he seconded this motion, he visualized that there were many members of the Massachusetts Medical Society who were capable of gathering and sifting this information and disseminating it for the benefit of the rest. He said that the Committee on Maternal Welfare was a precedent for the action proposed.

The motion to establish such a committee was defeated by vote of the Council.

Dr. Alexander A. Levi, Middlesex South, was recognized by the chair. He read Section 2(b), of Chapter V, of the by-laws as follows:

The secretary of a district society shall receive an application from a graduate of a discontinued medical school, a foreign medical school or any medical school not approved by the Council only when:

The applicant has possessed a license to practice medicine in the United States or its territories for at least five years. . . .

He offered as an amendment to this section the following:

The applicant has possessed a license to practice medicine in the United States or its territories for at least five years, termination of the elapsed time to be based on the date of the next censors' meeting. . . .

This amendment was seconded by Dr. Hyman Morrison, Norfolk.

Dr. Levi went on to say that, under the present by-law, the applicant covered by Section 2 (b), of Chapter V, might actually have been in practice five and a half years before he became eligible to apply for membership. He said that he would like to see this situation changed so that the five years would be calculated as running from the time of licensure to the date of the censors' examination. He added that if his amendment prevailed an applicant could apply in the regular manner on or before September 15 provided his waiting period of five years would be over before the censors' examination was scheduled to take place in the following December.

The Secretary said he knew the situation that Dr. Levi had in mind to change. He felt, however, that the language of the amendment, as submitted, could be improved on so that its meaning would be clearer and unmistakable.

On a vote by the Council, the motion to amend the by-laws was lost.

Dr. Chapin was recognized by the chair. He made the following motion:

That the President of the Massachusetts Medical Society be instructed to use such means as he sees fit to investigate and report to the next meeting of the Executive Committee the question of the young returned medical officer assigned to duty in the military hospital versus the medical officer already established there but suitable for overseas service.

This motion was seconded by Dr. Conley.

In supporting his motion, Dr. Chapin said he had written a letter to the Secretary on this matter. He spoke of two young doctors who had returned from overseas and who had been assigned to a base hospital on limited service. He complained that these young men are not given the type of work they are trained to do. He added that the Commanding Officer of this hospital has an excellent setup but that the officers he has trained might well be suitable for overseas service, which would permit more advantageous placement of returned officers.

Dr. Lund thought it would be embarrassing for the Society to make any move in the way of asking the Army to look into the special cases of young men who are not getting the kind of work they like. Dr. Chapin said that what he desired was that these returned officers be used to some purpose and that they be made to feel that they are doing good medicine again.

At that point in the discussion, the President said that he would be very much confused about his duties as outlined in this motion. He said that he was a little in doubt how and where he should proceed to get the information for the Council. He added, however, that it was the President's duty to do what the Council asks him to do.

On a vote by the Council, the motion was lost.

Dr. Hornor moved that the Council adjourn. This motion was seconded by Dr. Lund, and it was so ordered by vote of the Council.

The President declared the Council adjourned at 2:00 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE OF COUNCILORS

BERKSHIRE

I. S. F. Dodd
C. F. Kernan
Solomon Schwager
P. J. Sullivan

H. R. Kurth

P. J. Look
R. C. Norris
G. L. Richardson
F. W. Snow
C. F. Warren

BRISTOL NORTH

W. H. Allen
J. H. Brewster
R. M. Chambers
W. J. Morse
J. L. Murphy
W. M. Stobbs

ESSEX SOUTH

Bernard Appel
H. A. Boyle
D. S. Clark
Loring Grimes
P. P. Johnson
B. B. Mansfield
W. G. Phippen
E. D. Reynolds
H. D. Stebbins
P. E. Tivnan
J. W. Trask
C. F. Twomey
C. A. Worthen

BRISTOL SOUTH

G. W. Blood
R. B. Butler
E. D. Gardner
P. E. Truesdale

ESSEX NORTH

E. S. Bagnall
R. V. Baketel
J. T. Batal
G. J. Connor
Elizabeth Councilman
E. H. Ganley

FRANKLIN

H. M. Kemp

HAMPDEN

E. P. Bagge
M. J. Bachulus

W. A. R. Chapin
A. J. Douglas
J. E. Dwyer
Frederic Hagler
A. G. Rice
G. L. Schadt
J. A. Seaman

HAMPSHIRE

W. M. Dobson

MIDDLESEX EAST

J. H. Blaisdell
Richard Dutton
E. M. Halligan
R. W. Layton
M. J. Quinn
R. R. Stratton

MIDDLESEX NORTH

W. M. Collins
D. J. Ellison
H. M. Larrabee
W. F. Ryan
M. A. Tighe

MIDDLESEX SOUTH

C. F. Atwood
E. W. Barron
Harris Bass
J. M. Baty
J. D. Bennett
G. F. H. Bowers
Madeline R. Brown
R. W. Buck
E. J. Butler
J. F. Casey
C. W. Clark
B. F. Conley
H. F. Day
J. G. Downing
C. W. Finnerty
H. Q. Gallupe
F. W. Gay
H. G. Giddings
H. W. Godfrey
J. L. Golden
Eliot Hubbard, Jr.
F. R. Jouett
E. E. Kattwinkel
A. A. Levi
F. P. Lowry
A. N. Makechnie
J. C. Merriam
C. E. Mongan
J. P. Nelligan
E. J. O'Brien
Dwight O'Hara
Fabyan Packard
L. G. Paul
Max Ritvo
E. H. Robbins
M. J. Schlesinger
E. W. Small
H. P. Stevens
K. J. Tillotson
A. B. Toppan
Fresenius Van Nüys
C. F. Walcott
A. L. Watkins
Hovhannes Zovickian

NORFOLK

Carl Bearse
Arthur Berk
M. I. Berman
J. H. Carey
D. J. Collins
William Dameshek

G. L. Doherty
Albert Ehrenfried
H. M. Emmons
J. C. V. Fisher
Susannah Friedman
B. A. Godvin
J. B. Hall
H. B. Harris
R. J. Heffernan
P. J. Jakmauh
I. R. Jankelson
C. J. Kickham
C. J. E. Kickham
H. M. Landesman
D. S. Luce
C. M. Lydon
H. L. McCarthy
F. J. Moran
Hyman Morrison
D. J. Mullane
Abraham Myerson
M. W. O'Connell
W. R. Ohler
G. W. Papen
S. A. Robins
D. D. Scannell
Kathleyne S. Snow
J. W. Spellman
M. H. Spellman
N. A. Welch

NORFOLK SOUTH

C. S. Adams
F. A. Bartlett
D. L. Belding
Harry Braverman
H. A. Robinson
D. B. Reardon

PLYMOUTH

S. J. Beers
J. J. McNamara
G. A. Moore
B. H. Peirce
W. H. Pulsifer

SUFFOLK

W. E. Browne
David Cheever
Pasquale Costanza
G. B. Fenwick
Reginald Fitz
Maurice Fremont-Sn
Joseph Garland
R. L. Goodale
John Homans
A. A. Hornor
L. M. Hurxthal
R. I. Lee
C. C. Lund
Donald Munro
H. L. Musgrave
H. F. Newton
R. N. Nye
F. R. Ober
F. W. O'Brien
J. P. O'Hare
Helen S. Pittman
J. J. Regan
H. F. Root
R. M. Smith
M. C. Sosman
E. F. Timmins
J. J. Todd
S. N. Vose
Conrad Wesselhoeft

WORCESTER

C. R. Abbot
A. W. Atwood

George Ballantyne
Gordon Berry
W. P. Bowers
E. J. Crane
John Fallon
L. M. Felton
E. R. Leib
L. P. Leland
W. F. Lynch
J. C. McCann
A. E. O'Connell
J. C. Sullivan

R. J. Ward
R. P. Watkins
B. C. Wheeler

WORCESTER NORTH

H. D. Bone
C. B. Gay
G. P. Keaveny
J. V. McHugh
F. A. Reynolds
B. P. Sweeney

APPENDIX NO. 2

REPORT OF THE EXECUTIVE COMMITTEE OF THE COUNCIL

The Executive Committee, in the name of the Massachusetts Medical Society, endorsed the Fifth War Loan Drive and referred a telegram from Dr. Olin West, secretary of the American Medical Association, concerning it to the Society's Committee on Finance.

A question arose in the Committee as to the legality of the Council's action in May, 1944, in adopting one of the recommendations contained in the report of the Committee on Medical Information Bureau. This recommendation had to do with an appropriation of \$2500, which was granted by the Council for the use of the committee. It was contended that the recommendation should have been first submitted to the Committee on Finance; failing in this, the Council should have made the appropriation contingent on its approval by this committee. The Executive Committee, taking notice of the general demand in the Society for the prosecution of the work of the Committee on Medical Information Bureau, instructed the President and Secretary to examine this situation. In the event that the appropriation had been improperly made, the President was urged to exercise his emergency powers so as to make this money available. Subsequently, each member of the Executive Committee was in receipt of an opinion on this matter written by the President. In substance this opinion is to the effect that there is inherent in several sections of the by-laws manifest evidence that it is the intention to have the Committee on Finance scrutinize any proposals for the expenditure of monies which are extraordinary or other than routine. The opinion goes on to say that there is also precedent for the appropriation of monies directly by the Council but this has been contingent on the appropriations approval by the Committee on Finance. The President has exercised his emergency powers and this money has been made available to the Committee on Medical Information Bureau.

The committee responded to a letter from Mr. Powell M. Cabot, Massachusetts director of the War Manpower Commission, asking that the Society set up machinery similar to that established for the purpose of aiding the Massachusetts OPA regarding rationing. This matter was referred to the War Participation Committee with instructions to co-operate with the Massachusetts War Manpower Commission. (The War Participation Committee will report on this matter later in this meeting.)

The Committee gave consideration to two additional communications, one from the Deputy Surgeon General of the United States Army and the other from the chief of the Procurement Division. They treat of the same subject and concern a change in policy in the office of the Surgeon General with regard to the commissioning of graduates of Middlesex University School of Medicine. I quote the pertinent part of the letter received from Deputy Surgeon General George F. Lull:

It is true that last December we stopped taking graduates of this institution [Middlesex] into the armed services. However, a few weeks ago we were approached by the dean of the school regarding seventy-five or eighty graduates of last year who had completed internships in accredited hospitals and who had been licensed to practice in Massachusetts. We told the dean that we would take these people, provided they were physically and otherwise qualified. You will see that the new rule can only apply to recent graduates, as they must have had accredited

internships, and those who have failed to pass the State Board will not be accepted.

The letter from Lieutenant Colonel Mark C. Elworthy, chief of the Procurement Division, concerns itself with the method by which graduates of Middlesex University School of Medicine, seeking commissions in the Army, will be processed in the future. This is as follows:

(1) Such a graduate must have a license to practice medicine in a state or territory and supply in proof of this a photostatic copy of his license.

(2) He must present evidence of completion of the four-year regular medical course and the possession of an M.D. degree: this evidence must be in the form of a letter from the dean of Middlesex University School of Medicine, testifying to applicant's completion of the four-year regular medical course and the possession of an M.D. degree.

(3) He must have had one year of rotating internship: in testimony thereof he must present a letter from the superintendent of a hospital approved for internship testifying to the fact that applicant completed at least one year of rotating internship. (An internship of nine months under the 9-9-9 program does not fulfill this requirement and is not acceptable.)

(4) He must have membership in a county or district medical society and present a photostatic copy of his current membership certificate or a certificate of an Army officer on active duty that he has personally examined such certificate and that it is satisfactory.

The last requirement may be waived if the applicant is in private practice and if he receives letters from three practicing physicians, graduates of approved schools and members of the district medical society where the applicant resides, testifying as to the applicant's ethical practice of medicine and professional qualifications. In lieu of this latter, the applicant may submit a letter from the secretary of the district medical society along the same lines. (The forms which these letters shall take are prescribed.)

In the event that the applicant is a graduate of Middlesex University School of Medicine and is in the process of serving an internship, in addition to the foregoing he must supply a letter signed by the chairman of the internship committee, by the superintendent of the hospital, by the chief of staff, by the chief of the medical staff and by the chief of the surgical staff. In no instance shall this letter be signed by less than three of such officers. (The form of the letter is prescribed.) This same regulation is in force for those graduates of Middlesex University School of Medicine who are hospital residents.

The Administrator of Veterans Affairs has advised that at this time only graduates of approved medical schools are acceptable for duty with the Veterans Administration Facilities. Therefore, physicians who are graduates of unapproved or substandard schools, including the Middlesex University School of Medicine, and who are physically qualified for duty only with the Veterans Administration Facilities, will not be processed. Any request to process such physicians will be returned to the Procurement Division with appropriate comments.

The Executive Committee has approved a plan submitted by the Red Cross for the training of volunteer nurse's aides in the treatment of infantile-paralysis patients in the noncommunicable stage of the disease. This matter was submitted to and approved by the Committee on Public Health of the Society.

The Committee reviewed the report of the Committee on Public Relations and approved the recommendations contained therein. (The Committee on Public Relations will report on this matter later in this meeting.)

The Executive Committee approved of certain ad interim appointments made by the President. (These appointments will be offered later in the meeting.)

MICHAEL A. TIGHE, Secretary

APPENDIX NO. 3

REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

The Committee on Public Relations held a meeting at the Harvard Club, Boston, on July 26. President Elmer S. Bagnall, President-elect Reginald Fitz, Secretary Michael A.

Tighe and representatives from ten districts attended. In addition, there were present, at the invitation of President Bagnall, Dr. Hugh F. Hare, president of the New England Roentgenological Society, Dr. Charles W. Blackett, chairman of the Executive Committee of that society, Dr. Merrill C. Sosman, past president of that society, Mr. Cahalane, executive director of the Blue Cross, Mr. Walter Amesbury, a director of the Blue Cross and administrator of the Waltham Hospital, and Dr. George A. MacIver, president of the Massachusetts Hospital Association.

The first business of the meeting was the consideration of the inclusion of payment for x-ray examination by the Blue Cross. After presentation by President Bagnall of the action of the House of Delegates of the American Medical Association and the House of Delegates of the American Hospital Association on this question there was free discussion. Each of the guests representing the Blue Cross and the New England Society of Roentgenologists spoke on the question. The general discussion was frank and open, and there was a clear picture in the minds of the committee when the guests left. When the discussion was ended, President-elect Reginald Fitz made the following motions:

(1) The Committee on Public Relations of the Massachusetts Medical Society does not now approve the proposed plan of Blue Cross to pay \$15 toward the costs of x-ray in hospitals.

(2) Discussion by the Massachusetts Hospital Service, Massachusetts Hospital Association, New England Roentgenological Society and Committee of the Massachusetts Medical Society to meet with the Massachusetts Hospital Association — Dr. Walter Phippen, Chairman — should be continued.

This motion was adopted by vote of the Committee.

The next business before the committee was consideration of the report of the subcommittee appointed to look into the possibility of better publicity for the Massachusetts Medical Society. A progress report was presented, the most important feature of which is that the Connecticut Medical Society has instituted an elaborate plan for publicity, which the committee is going to investigate and report on later.

Finally, the progress report of the Committee to Meet with the State Advisory Council of the Massachusetts Division of Unemployment Security was presented and accepted.

ALBERT A. HONOR, *Secretary*

APPENDIX NO. 4

SOME COMMENTS ON THE PROCEEDINGS OF THE MEETING OF THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION

The House of Delegates of the American Medical Association convened in the Red Lacquer Room of the Palmer House, Chicago, on June 12, 1944. The speaker of the House, Dr. H. H. Shoulders, called the meeting to order at 10.15 a.m.

The preliminary report of the Reference Committee on Credentials through its chairman, Deering G. Smith, of New Hampshire, indicated an early registration of 150 delegates. Later in the week a registration of 170 delegates was reported out of a possible 175. This wonderful registration was one of the highest recorded at a meeting of the American Medical Association. It included delegates from the several states, one delegate each from Hawaii, the Isthmian Canal Zone and Puerto Rico, one delegate from the United States Army, one from the Navy, one from the Public Health Service, and one delegate each from the several sections.

This remarkable assembly indicated a strong interest of the members in the work of the House and also indicated the deep responsibility of each member. It also showed an appreciation of the seriousness of the problems that concern organized medicine in the United States.

Members of the reference committees showed a fair distribution among the several states, the specialties and the special delegates. Two members of the Massachusetts Delegation were each given a place on a reference committee. Dr. Charles E. Mongan was appointed a member of the Reference Committee of Amendments to the Constitution and By-Laws, and Dr. Walter G. Phippen was appointed a member of the Committee on the Report of Officers. Together with the secretaries from other states, Dr. Michael A.

Tighe, secretary of the Massachusetts Medical Society, was granted the privilege of attending the meetings of the House of Delegates in executive session.

It would be impossible to give a detailed report of the proceedings of the House of Delegates at this meeting. Suffice it to say that the report of the proceedings of the House of Delegates would cover ninety-four pages of the *Journal of the American Medical Association*. Your reporter will endeavor to select a few of the most important items discussed and acted upon at this meeting:

On December 31, 1943, the official membership of the American Medical Association carried the names of the 123,586 members. There was a net gain of 1876 above the number of enrolled members of December 31, 1942.

The Treasurer's Report no doubt will interest some of our members. The total wealth of the Association is \$5,711,833.17. The total income in 1943 was \$1,186,544.26. The income in excess of the expenses was \$718,873.76.

The report of the Council on Medical Service and Public Relations shows that this body is one of the most important councils of the American Medical Association. It is a little over one year old, and it made its first report at the meeting in June. The main office of the council is in the Association building in Chicago. There was also established a Washington office of the Council on April 3, 1944. It is located at 1835 High Street, N.W. Dr. Joseph S. Lawrence, executive officer of the Medical Society of the State of New York, was secured as a consultant, and the development of the office was placed under his direction.

The Council on Medical Service and Public Relations will probably become one of the most important Councils in the American Medical Association. Already it is advocating the creation of a federal department of public health, which will have a place in the President's Cabinet and will have under its control all medical activities of the federal government. As long ago as June, 1892, a communication from Dr. Henry O. Marcy, of Cambridge, Massachusetts, was received by the Massachusetts Medical Society asking for its influence in the creation of a Cabinet office for public health in Washington. The American Medical Association today advocates the same procedure.

The Council on Medical Service and Public Relations has taken up the matter of jurisdiction of the Children's Bureau of the Department of Labor in regard to furnishing medical aid to the citizens of the United States.

Let me read a paragraph from the proceedings of the House of Delegates.

A very clear statement was made by a number of physicians representing the American Academy of Pediatrics and the American Medical Association, and by some medical members of the Advisory Committee, to the effect that physicians, while concurring in the purpose of the program to render service to and free from anxiety the families of servicemen, wished it understood that they are aware of the potentialities of this program as a possible trial balloon, bridgehead or entering wedge looking toward the extension of medical service in point of time beyond the duration of the war and in breadth of scope, both as to kinds of service and as to groups served. They served notice on the Children's Bureau that they would wholeheartedly co-operate with the program for servicemen's families for the duration but not beyond. In response, officials of the Children's Bureau stated that the program was carried on under the authority of the Social Security Act, but under temporary appropriations visualized as national defense appropriations and therefore terminating six months after the peace. As to what they might advocate after the peace, officials of the Children's Bureau refused to be committed. Miss Lenroot stated specifically that after the peace there would be opportunity for any group to advocate any kind of program, conservative or liberal, which it might choose. Dr. Eliot stated that the EMIC program as it stands was an outgrowth of the emergency and was undertaken in response to a request from an Army general at Fort Lewis, Washington. She added that it was not a part of any "master plan" of which she had knowledge.

Following this meeting the Children's Bureau issued a revised set of regulations, which were published in the *Journal of the American Medical Association* on January 22, 1944.

Contained in Title V of the Social Security Act is authorization for experiments and demonstrations in medical

care. It was this authorization which permitted the Children's Bureau to start the Washington State Health Department on an experimental program in emergency medical and infant care for servicemen's wives and children in the vicinity of Fort Lewis. This is cited by the Children's Bureau as its legislative authority for starting new programs. Existing funds can be and are being used, but when the program grows very large, as in the EMIC situation, additional appropriations are necessary. A program for the care of rheumatic children now being developed is based on this same authority in Title V of the Social Security Act. This was extensively discussed at a meeting on October 6 and 7 by a group including representatives of many public-health agencies and also including the Advisory Committee to the Children's Bureau. In approximately twelve states demonstrations in the care of rheumatic fever patients are being carried out through maternal and child health divisions of the state health departments. Presumably this program may be extended by adopting it in other states. At present it is limited to the care of those who are not able to procure treatment privately. It would appear that the Children's Bureau considers medical treatment to be an integral part of public-health service in many circumstances. Extension of the rheumatic fever program to other states and to broader population groups is a logical step in the extension of federalized medicine by those who believe that such procedures are in the public interest.

The resolution offered by the delegates from California, asking that a change be made in the office of secretary of the American Medical Association and also in the office of editor of the *Journal of the American Medical Association* was refused by a vote of 144 to 9, which was a very flattering endorsement of the work of Dr. West and Dr. Fishbein.

Your reporter would like to call special attention to the speeches of Dr. Shoulders, speaker of the House of Delegates, Dr. James E. Paullin, former president, President Herman L. Kreisler and Dr. Frank H. Lahey.

I recommend that you studiously read the reports of the House of Delegates as reported in the June 24 and July 1 numbers of the *Journal of the American Medical Association*.

The Massachusetts Medical Society has contributed greatly to the promotion of sound underlying principles which act as guides to its members in the practice of medicine. The Society has given to the public sound advice as to public health and prevention of disease. It has furnished from its society members four presidents of the American Medical Association, namely, Dr. Henry I. Bowditch, Dr. Henry O. Marty, Dr. Herbert L. Burrell and Dr. Frank H. Lahey. Another member of the Society has been called to the presidency of the American Medical Association. He is especially equipped for the office and well informed as to the nature of the problems confronting organized medicine. He was a member of the House of Delegates for ten years. He was a member of the Board of Trustees for five years, having been its chairman. He is a practitioner of medicine and was formerly president of the American College of Physicians. Outside the field of medicine he has been for many years one of the administrators of one of the largest universities in the United States. He brings to the office outstanding ability in the way of large vision, capacity and rare executive ability. With such a record, I think you will agree with me when I say that Dr. Roger I. Lee is eminently qualified to be the president of the American Medical Association.

CHARLES E. MONGAN, *Senior Delegate*

APPENDIX NO. 5

REPORT OF THE SUBCOMMITTEE ON POSTPAYMENT MEDICAL CARE (BANK PLAN)

I am presenting this report to the Council without a meeting of the full committee having been held. For this I deeply apologize. My understanding was that nothing was to be said or made public about the plan until it was released by the American Bankers Association, with the consent of your committee. This was not to be completed in all details until some time about the middle of this month. Two days ago, however, I received a note with an enclosure from our good president requesting me to incorporate certain lines from the enclosure in my report to the Council. I, therefore, offer this report at this time not only with my apologies to the

entire committee but with my assurance to them that, as soon as the releases come through from the A.B.A., a meeting of the full committee will be held wherein they will be given an opportunity to offer suggestions or criticisms so that we may at the February meeting of the Council present our final suggestions and opinions on this subject.

As you all know, the spade work was done by the original committee under the able chairmanship of Elmer Bagnall, our president.

This plan was first devised by the Massachusetts Bankers Association, through its Consumer Credit Commission. It has been approved by the Council and is available to all banks in Massachusetts. It is proposed as a supplement to the Blue Cross and the Blue Shield.

The small-loan divisions of all banks in this state, as well as the small-loan companies, find that the second and third most frequent reasons given by people when applying for loans is for the payment of medical services. Obviously a real need exists for this plan. Let it be understood that the rates charged for this plan are low and easily explained. The charges are either added to or included in the doctor's fee. The patient signs a note for the agreed amount payable in six, eight, ten or twelve installments. A simple credit application is obtained, which the doctor or his secretary telephones to the bank. The facts are checked by the bank and the doctor is notified when the note is approved. In due course the signed note is presented by the doctor to the bank for discount. To secure the doctor and the bank against loss a reserve is set up out of each account on the books of the bank in the doctor's name. The need for the reserve depends on the credit of the patient and on the doctor's practice. By agreement, the reserve may be increased to cover even marginal situations, although the usual reserve will be about 10 per cent. It is paid to the doctor customarily as payment of each account is completed. As a result of the reserve feature the advance by the bank is lessened and the term of its payment is shortened so that the yield on the suggested rates compares closely with that of personal loans.

Whereas we are told by the banking interests that well over 90 per cent of all small loans issued by them are paid and whereas this gives us the assurance of collection by the bank's business methods, it must be understood that this plan is in no way the procedure of a collection agency. It is simply a method of making it easier for a man who eventually pays his bills to satisfy the legitimate claims of the physician and to relieve him and the doctor of repeated monthly statements. It will take time for the plan to become the customary procedure. Over the years its use will expand.

There are several brochures and pamphlets which are being passed around among you today which are connected with this plan. Your committee, when it first considered the expense of putting this plan over, felt that it might well have to be abandoned because of this factor. The minimum cost, it seemed to us, would be about \$600. None of us had the courage to come before this body and ask for that amount of money. When Mr. McCarthy, of the National Shawmut Bank, presented his plan to the American Banker's Association, however, they agreed to underwrite the expense of all the brochures, literature and publicity and to collect a proportionate amount of this expense from the member banks in this state. Massachusetts is the guinea pig. If the plan works out well here it will be extended to all the states in the union. Again, members of the Council, Massachusetts, there she stands!

I am going to close this report here, because I think that any details that may have been omitted can be better brought out in answering questions. And in doing this I shall not hesitate to call on Dr. Bagnall for assistance.

DANIEL J. ELLISON, *Chairman*

APPENDIX NO 6

REPORT OF COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL CARE COSTS INSURANCE

An interim report on the progress of Massachusetts Medical Service is presented for your consideration.

SUBSCRIBER ENROLLMENT

It is approximately two years since you took the final steps that launched the corporation for prepaid medical care.

The growth since that time has been steady and progressive so that we are on a par with or ahead of the older plans in the country, excepting those of California and Michigan.

TABLE 1. *Blue Shield Enrollment.*

MONTH	NO OF CONTRACTS	NO OF PARTICIPANTS
1943		
January	123	230
February	216	428
March	257	503
April	193	396
May	101	217
June	386	868
	1,276	2,642
July	666	1515
August	579	1102
September	901	2262
October	1928	4435
November	2616	5726
December	2320	5486
	9,010	20,526
1944		
January	798	1795
February	597	1196
March	1599	3703
April	973	2356
May	838	1839
June	1293	2996
	6,098	13,885
July	1354	2782
August	1852	4006
September	2258	4808
	5,464	11,596
Gross enrollment (Sep- tember 30, 1944)	21,848	48,649
Cancellations	3,037	7,305
Net enrollment (Sep- tember 30, 1944)	18,811	41,304

Table 1 presents interesting data on growth. I shall simply note the high spots. As of January 1, 1943, we had enrolled 230 subscribers; in June, 1943, there were 2642 subscribers; at the turn of the year, in early 1944, there were 23,168 subscribers; in June, 1944, there were 37,053 subscribers; and as of September, 48,649 subscribers had been enrolled. The term subscriber means total participants in family groups. Actually, 21,848 contracts have been sold, so there is an average of 2.2 persons per contract in force.

Of considerable interest is the fact that during this period there were cancellations of 3037 contracts covering 7345 participants. This leaves a net enrollment in September of 41,304 participants on 18,811 contracts in force. These are distributed among 572 groups. These facts have just come to our attention and should be looked at critically and carefully. It must be done, however, with astuteness and without allowing precipitate action, because cancellations are a characteristic of the early history of all plans. Michigan had a complete cancellation by its original big sponsor, the Ford Motor Company, yet it went on and has enrolled 600,000 subscribers in the last four years. They were not panicked away from their basic concepts, which they had learned were correct because of such cancellations.

FINANCES

On the financial side we have been most fortunate. Table 2 portrays what has happened during this period. The figures are arranged in vertical columns that give the percentage distribution of funds for various items. Of great importance are the extreme variations in the percentages of the premium payments distributed to physicians. They vary from a low figure of 17.1 per cent to a high figure of 84.2 per cent. The corresponding figures for funds allotted to unrestricted surplus vary in a parallel fashion, the highest being a generous deposit on 68.2 per cent, and the lowest a deficit of 22.7 per cent, which occurred during the early days of the corporation. This means but one thing. Our experience today is so far from being stabilized that any significant departure from our present basis for disbursing funds would probably constitute poor business judgment. New factors coming into the picture may account for this fluctuation: tonsillectomy is the largest single item in all medical plans and comes in irregularly by seasons, with a year's waiting period; obstetric services are probably just now coming in significantly since there is also

a waiting period of one year for this type of medical service and, finally, six months ago all restrictions regarding pre-existing conditions were removed.

Our administrative costs, based on a contractual relation with the Blue Cross, have shown a steady decline until now they have reached the low figure of 13 per cent. You will recall that I have said at other times that it has been e-

TABLE 2. *Distribution of Blue Shield Funds.*

DATE	PAID TO PHYSICIANS	OPERATING COSTS	CREDITED TO LEGAL RESERVE	UNRE- STRICTED SURPLUS	CASH HANDLED
	%	%	%	%	
To August, 1943	34.0	94.7		-28.7	-\$2,844
September	25.3	37.3		37.4	
October	17.1	15.7		67.2	
November	18.2	13.6		68.2	
December	27.4	26.5		21.1	
To January, 1944	32.3	39.0		3.7	\$10,387
January	24.7	16.1		34.2	
February	46.2	16.4	25.0	12.4	
March	37.2	13.2	25.0	24.6	
April	46.2	14.3	25.0	14.5	
May	64.9	13.2	25.0	-3.1	
June	29.2	13.4	25.0	32.4	
To June, 1944	41.7	13.9	25.0	19.4	\$45,369
July	84.2	13.5	25.0	-22.7	

estimated that to administer a medical-service plan with joint contracts with the Blue Cross would require about 25 per cent of the premiums. Our expense for administration will show an increase in the immediate future. At the request of the Blue Cross, one of their employees, Mr. E. J. Cunningham, has been assigned full time to Blue Shield, and his services will be charged completely against us. In the future the services of a physician to help in reviewing claims will have to be engaged; for the past two years I have worked with the claim department, of course without charge, so that we might get on our feet financially.

We have done satisfactorily to the extent of having an unrestricted surplus of \$46,571.62. These funds must be conserved so that eventually we can include hospital medical care. It is the ruling of the Commissioner of Insurance, at least to date, that we cannot reimburse the society its \$25,000 until we have accumulated a surplus of \$255,000 surplus. At that time the requirement that 25 per cent of premium must be placed in a legal reserve that cannot be touched will also be removed.

CURRENT PROBLEMS

There are, of course, and probably always will be, the so-called "current problems." These problems, however, have been at an absolute minimum in Massachusetts as compared with the experiences encountered in other parts of the country. One hears an occasional disparaging remark, but the total overall interrelation between the profession, the subscribers and the Blue Cross has been healthier here than in any other place in the country, with due consideration of our size. So if minor problems present themselves, we should be shortsighted to precipitate ourselves into unwise action and departures.

Subscriber satisfaction has been hard to measure. It will never be 100 per cent. Our cancellations bear that out. The provision for nonpayment to nonparticipating physicians has been the chief cause of complaint. A few groups have said that the total cost for hospital and surgical contracts when combined is rather high. Nonpayment for nonhospitalized surgical conditions has been sometimes objected to. Absence of good faith on the part of participating physicians who agreed in a signed contract not to make additional charges to the under-income group but who have done so, even to the extent of charging as much again as the corporate plan allowed, has rightly caused mistrust of our purpose on the part both of the subscriber and of the industry in which he works. Nonparticipation or open criticism by industrial physicians has kept groups from joining.

Dissatisfactions among the profession have arisen at times but for the most part have been satisfactorily handled.

The fee schedule has been the source of some misunderstandings. By and large it has been considered to be equitable and fair. Certain individual items have not been fairly estimated. At my suggestion, and with the approval and instruction of the Board of Directors, all sections of the schedule will be restudied by committees appointed in the different specialties, and an effort to arrive at a fully acceptable revised schedule will be made. There of course cannot and will not be any general upward revision of the schedule. We may as well quit tomorrow as ask the subscribers to pay larger premiums, not for an increase in benefits, but for a larger stipend to physicians. This work, if accurately done, will take some time. Suggested changes must be weighed against our actual experience before being put into practice, to allow us to continue to operate in the black. Operating in the red, with consequent reduction in professional fees, has been the chief source of turmoil in other state societies; this we have been spared, only because we have operated in the black.

There are, of course, administrative problems. In the past there have been delays in paying doctors, but an attempt to correct this has been made by authorizing immediate payment of claims once they are cleared, rather than paying once a month. The service report has been revised so as to require less work. There is often a delay, up to six weeks or more, before the physician knows he has a Blue Shield case on his hands. This is sometimes due to delay on the part of the hospital in reporting a Blue Cross subscriber, whereby the corporation can tell from its files that the patient is also a Blue Shield subscriber, and so notify the physician. Much of this difficulty could be immediately eliminated if the hospitals would comply with a simple request I presented many months ago for their approval; namely, that the Blue Cross admitting form have a simple Blue Shield stub attached, on which the hospital admitting officer can write the patient's name, if a Blue Shield subscriber, and the doctor's name, tear the stub off and present it to the doctor. But all good things come slowly. Even that would not correct one situation in which a participating physician has in his drawer eleven incomplete forms, which he refuses to send in even after several letters from Boston.

PARTICIPATING PHYSICIANS

The final key to our success is the participation in this program by the bulk of the profession. If they come in, we must succeed; if they do not, we must inevitably fail with all the consequences entailed. Up to April, 1943, there were 3283 participating physicians; in the next year and three months, 294 more physicians had enrolled; and in the last three months (July, August and September), 86 more physicians have enrolled, giving a total of 3663 physicians. Withdrawals have been negligible. If the generous allowance of 5000 physicians in actual practice is taken, then 75 per cent of them are participating.

Why we need full support is clearly demonstrated by one experience. One large firm with over 2000 potential subscribers was considering the Blue Shield; they operate in the metropolitan area of Boston. They appointed a group of company officers to investigate participation. Their conclusion was that until free access to all hospitals and specialties was assured in the Boston area by a broader participation of physicians than now exists they would not join the Blue Shield.

Why is it that men refuse to support the effort of their own society in a co-operative endeavor with public bodies? Do they not see the dangers ahead?

Yes, it is true that, as they say, wages are high. But so is the cost of living, and those families under the established income limits are having a harder time and need the service more than ever before.

Yes, it is a fact that we are now prosperous. But every one talks in terms of retrenchment in the coming years. Then both the people and the profession will be fortified against adversity if this program is as widely used as the Blue Cross.

Yes, it is true that a man likes to feel that he can charge what his services are worth, even to the low-income group. But if a man's colleagues who are equally equipped as himself consider this program fair, why is it that he should expect a larger fee, particularly when it jeopardizes a patient's financial integrity or forces the patient from a self-support-

ing to a charity service. What solid ground has he to stand on if he quotes Chicago spokesmen to the effect that physicians deal fairly with patients by scaling fees downward according to their means, when his local colleagues say that he is a major cause of some of our troubles by scaling his charges inconsiderately upward, regardless of the burden on the stricken patient, so as to maintain a personally established and personally supervised scale of values.

Yes, it is a fact that no law has yet been passed that places medicine under governmental supervision. But the present administration will certainly continue its efforts for such medical legislation; furthermore, the opposing candidate has called for extension of social-security protection in medical care. And do not forget that the mechanism must be insurance on the same basis as that for unemployment—compulsion. Mayor LaGuardia has initiated a program with the full support of the industrial giants in his territory covering income groups up to \$5000. The conservative party of England has presented its own social-security program, which in essence is identical with that of Beveridge; Canada has nearly completed its program for socialized medicine. The United States Chamber of Commerce has recently voted approval of governmental provision of medical care for workers, in the event that industry fails to do so on a voluntary insurance basis. *Our only weapon against this current is the plea, Let's do it on a voluntary basis!* Yet some physicians refuse to co-operate. If a sufficient number continue to hold out we shall fail. Who, then, do these physicians think are going to fight for their rights—the large number of men who have made these efforts to date? No indeed! As a body, I think that they may decide that further effort is futile. It behooves the Massachusetts Medical Society to work ardently to see that its full membership participates in this program.

* * *

Finally, there is one matter on which I ask action. In probably an unorthodox fashion, the Committee Concerned with Prepayment Medical-Care Costs Insurance was continued after its work had been completed. With the incorporation of Massachusetts Medical Service, it really had no further standing. I used it as a means whereby I, its president, could bring you periodic reports of progress. That has worked well, and I believe that, in the future, the President, if a physician, should be allowed the privilege of your rostrum. At this point I should point out that the by-laws adopted by you do not provide that the president shall be a physician. We who studied the problem thought that he should be and probably would be a physician. We left it unspecified, however, so that if, in the distant future, there were solid reasons for having a layman as president, that could be done. At any rate the control of the by-laws with reference to such matters rests wholly in the hands of the voting members—the Executive Committee of the Society.

Let us clarify the picture by discharging a committee that has completed its work. Provided that a physician will be president during the evolution of the program, I assume that some proper way under the rules of procedure will be found to permit him to make periodic reports to the Council in behalf of the entire profession.

JAMES C. McCANN, *Chairman*

APPENDIX NO. 7

REPORT OF THE COMMITTEE ON EXPERT TESTIMONY

A special committee to consider medical expert testimony as given in courts was appointed by the president of the Massachusetts Medical Society in 1936. The original committee consisted of Drs. David Cheever, Francis P. McCarthy, Walter Phippen, J. J. Goodwin and George L. Schadt, chairman. The present committee consists of Drs. David Cheever, William Brickley, Francis P. McCarthy, Carl Bearse and Frank R. Ober, chairman.

The present committee held its first meeting two years ago and has met several times since to discuss the problem of medical expert testimony. It has become apparent to us that the duty of a special committee appointed to consider

medical testimony in courts is to report its findings and make recommendations to the Council of the Massachusetts Medical Society. Your committee has studied a mass of material which has been recently published covering many fields of legal medicine. It has studied recent articles published in medical journals on this subject, and there has been correspondence with some of the state medical societies which have organized plans adopted to their situations.

California and Minnesota have established permanent committees on medical expert testimony, and the Minnesota committee collaborates with a similar one from the state bar association.

It must be stated, however, that the Massachusetts Medical Society has not been remiss in this matter since two of our standing committees — the Committee on Medical Defense and the Committee on Ethics and Discipline — have settled many such problems for several years. These two committees have their special functions, which entail a good deal of work, so it does not seem wise to overload these two bodies with a job which may not necessarily come into their province.

Medical expert testimony is in a constant and changing fluid state. In every case in which a physician is involved, there may be a problem to be solved by the medical profession. We as a group are concerned with ordinary as well as expert testimony. Testimony may be given in hearings, before industrial accident boards, before judges and before juries, when grievances occur or when there are trumped-up cases. There should be some new permanent machinery set

up by the Society in order that the testimony of poor or bad witnesses may be reviewed and suitable methods advised for correction or for disciplining the offending medical witness, or lawyer, or both.

This committee should be a standing one. The Massachusetts Bar Association might be invited to set up a similar committee among its members, and these committees should be given authority to collaborate. It is important that the committee be a standing one. It should also collaborate with the Committee on Ethics and Discipline and the Committee on Medical Defense. All cases with evidence of bad testimony should be heard and investigated by such a committee, which should be empowered to make recommendations to the Committee on Ethics and Discipline.

The functions of a standing committee on medical expert testimony should be twofold: first, punitive and, second, educational. It should set up a program of education for the physicians. It should collaborate with all the parties concerned, and above all it should not endeavor to solve all the many controversial problems at once.

This special committee therefore recommends:

(1) That a standing committee of five or more, to be called the Committee on Medicolegal Problems, be appointed by the President.

(2) That the by-laws of the Massachusetts Medical Society be amended to provide for such a body.

FRANK R. OBER, *Chairman*

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 30511

PRESENTATION OF CASE

A seventy-six-year-old woman was admitted to the hospital because of abdominal pain.

Five days prior to admission, while sitting quietly in the evening, the patient felt a rather severe colicky pain below the left breast just outside the midline. This disappeared during the course of the night, and for the next two days she felt well and was fairly active. Two days before entry the pain recurred in the epigastrium and was intermittent in character. A physician prescribed some pills; these made her feel nauseated, but she did not vomit. On the same day she had a bowel movement; this was followed by constipation, which failed to yield to a saline cathartic. On the day before admission the pain shifted to the right lower quadrant. It was constantly present and was aggravated by movement in bed. The temperature rose to 101°F. There was no vomiting or cough.

For six and a half years prior to entry the patient had been known to have hypertension, with pres-

ures of 160 to 170 systolic, 100 to 110 diastolic. Six months before admission the blood pressure was 190 systolic, 100 diastolic.

Physical examination revealed an acutely ill woman. There was exquisite tenderness over the right half of the abdomen, which was thought to be most marked in the right upper quadrant over the gall bladder. Practically no muscle spasm was present. Palpation in the right lower quadrant produced pain referred to the left lower quadrant. Tenderness in the right costovertebral angle was demonstrable when she lay on her back, but this disappeared when she turned on her right side. The psoas sign was negative. There was no rectal tenderness.

The temperature was 101°F., the pulse 88, and the respirations 24. The blood pressure was 190 systolic, 90 diastolic.

Examination of the blood revealed a white-cell count of 18,000, with 80 per cent neutrophils. The hemoglobin was 15.8 gm. per 100 cc. The urine had a specific gravity of 1.032, with a ++ test for albumin and a sediment containing 15 white cells, 25 epithelial cells and an occasional granular cast per high-power field. The serum nonprotein nitrogen was 47 mg. per 100 cc., and the blood sugar was normal.

Two hours after admission a cholecystectomy was performed under ether anesthesia. A tense, distended, edematous gall bladder surrounded by recent inflammatory adhesions was found. It had a queer yellowish color, with greenish areas, and appeared unlike any acute gall bladder that the surgeon had seen in the past. The common duct was apparently of normal size. The head of the pancreas was normal to touch but not entirely normal in appearance; there was no fat necrosis.

*On leave of absence.

The pathological report was acute and chronic cholecystitis.

Following operation the patient was quite drowsy, although she received little medication. She continued to complain of pain on the slightest movement. An electrocardiogram revealed auricular premature beats but no evidence of heart disease.

On the afternoon of the third postoperative day the patient suddenly became dyspneic and cyanotic, although the lungs remained clear. The blood pressure fell, and she became stuporous, failed to recognize her family and expired about three hours after the onset of the acute episode.

DIFFERENTIAL DIAGNOSIS

DR. REGINALD H. SMITHWICK: We have a woman in the older age group who was operated on approximately one week after the onset of symptoms, an acute near-gangrenous gall bladder being removed. She died suddenly a few days following operation and three hours after the onset of an acute episode consisting of dyspnea, cyanosis and low blood pressure. The questions seem to be, What was the cause of death, and did the acute gall bladder represent the full extent of the pathology?

Certain symptoms, signs and laboratory data are given. The first symptom was pain, apparently quite severe and sudden in origin, located in the left anterior chest at about the level of the sixth or seventh dorsal vertebra and to the left of the midline; it lasted several hours and never recurred. Such a pain might have arisen from pathology in a thoracic organ, such as the heart, the lung or the aorta, but no evidence of cardiac or pulmonary disease was noted. It could have been referred pain from an upper abdominal viscus, such as the pancreas or gall bladder, but that, although wholly possible, is unusual. After two days without symptoms the onset of epigastric pain, intermittent in character, was noted. This was associated with nausea and constipation, and after twenty-four hours shifted to the right lower quadrant. Following this it was continuous, aggravated by motion and associated with fever, an elevated white-cell count and marked tenderness over the right abdomen, maximal over the gall-bladder region, with practically no spasm. All this seems consistent with the finding at operation of an acutely inflamed, distended gall bladder. It is rather surprising, however, that no mass was felt in view of the absence of spasm, and the pain on motion is a little more marked than one would expect since pain at this stage of acute infection of the gall bladder is usually associated with spasm and a mass due to the implication of the omentum and colon by local peritonitis. One gathers the impression that the surrounding peritonitis was not marked, since the gall bladder was removed, the common duct said to be normal in size, and the head of the pancreas normal to palpation but not in appearance. The latter

suggests the possibility that some form of pancreatitis also existed. An extension of this process subsequent to operation might explain the persistence of pain on motion following operation, — I assume that pain from the incision was discounted, — the drowsiness of the patient, owing to toxemia, and the sudden death with dyspnea and cyanosis and circulatory collapse without evidence of pulmonary or cardiac disease.

One might speculate regarding other possibilities. In a woman of this age, with systolic hypertension, indicating disease of the large blood vessels, vascular accidents may be expected. I am inclined to discount the moderately elevated nonprotein nitrogen as being the result of dehydration and hemoconcentration and to exclude uremia as a cause of death. There seems to be no good evidence of a cerebral accident or coronary thrombosis. Other vascular accidents, such as thrombosis of the mesenteric vessels and rupture of a blood vessel, also seem unlikely, although the possibility of dissecting aneurysm should be mentioned, largely because of the sequence of symptoms: first, thoracic pain, then, upper abdominal pain and, finally, lower abdominal pain. The unusual appearance of the gall bladder, which was tense, distended, edematous and yellowish rather than the more usual reddish purple, with greenish areas, was probably the result of the proper combination of obstruction, infection and the transudation of bile pigments into the wall. I have seen a few somewhat similar acute gall bladders. In a patient of this age group, pulmonary embolism is a possible cause of death, but it seems as if some physical signs, such as distended neck veins and pulmonary edema, pointing to this should have developed in three hours. This is also likelier to cause death after a longer interval following operation. Rupture of a dissecting aneurysm into the pleural or pericardial cavity usually results in death in a few minutes rather than in hours. Hepatic insufficiency seems unlikely in the absence of jaundice. Adrenal insufficiency due to hemorrhage into the medullas of the adrenal glands is a rare cause of death with circulatory collapse.

A rapidly progressing pancreatitis following the acute cholecystitis seems a possible explanation for the persistence of abdominal pain and the continued downward progress of this patient after operation, with sudden death forty-eight hours later.

DR. HELEN PITTMAN: This woman had had hypertension for six and a half years. She was an extremely active woman for her age. When I first saw her she was unusually well. I could never make any diagnosis except for a certain amount of arteriosclerosis and hypertension. In the last year she had been aging rapidly. I saw her about three months before admission, and at that time she had lost her vitality, tired easily and had more hypertension, but nothing new. I did not hear from her again until seven o'clock in the evening of admission. I was

struck by the fact that she had severe pain. She was a person who had always been well and who had never been a complainer, and she was obviously in extraordinarily severe pain on the slightest motion. There was exquisite abdominal tenderness without spasm or with so little spasm that it was disproportionate to the amount of tenderness. I called for Dr. McKittrick, and the rest of the story is his.

DR. LELAND S. MCKITTRICK: Dr. Smithwick gave an excellent discussion, and I was pulling hard hoping that he was going to take a long shot and make the correct diagnosis. He made the logical one, however.

I did not know what this patient had. I would not have operated if I could have been sure that she did not have an early rupture of the gall bladder. It seemed that tenderness was definitely present in the gall-bladder region, and whereas we suspected acute cholecystitis, I was not sure enough of the diagnosis to refuse operation.

It was a queer looking gall bladder and was as described in the abstract. I did not attempt to describe the appearance of the pancreas because I could not. It just did not look normal even though it felt all right. There was no fat necrosis. I was fairly sure that the patient did not have an acute hemorrhagic pancreatitis. We took the gall bladder out and did not think too much about it until I opened it and did not find any stones. I commented to the small but select group assembled at one o'clock in the morning that I had not seen more than one or two acute gall bladders that did not contain a stone. I was worried about it. I did not notice anything abnormal in the liver.

We finished the operation but were unhappy in our minds, thinking probably that this was one of those conditions for which we do not know the explanation and that it was an acute cholecystitis. I did not know what happened postoperatively except that she died, and I was totally ignorant about what was going to be found until I saw the autopsy.

CLINICAL DIAGNOSIS

(Acute cholecystitis.)

DR. SMITHWICK'S DIAGNOSES

(Acute cholecystitis.)

Acute pancreatitis.

ANATOMICAL DIAGNOSES

Thrombosis of celiac axis and hepatic, cystic, superior mesenteric and splenic arteries.
 Infarction of liver, spleen and intestine.
 Arteriosclerosis, severe, generalized.
 Cardiac hypertrophy, hypertensive type.
 Pulmonary emboli, multiple, small, recent.
 Operation: removal of gangrenous gall bladder.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: When the abdominal cavity was opened, the striking finding was early gangrene of the entire small intestine and part of the right colon. The infarction was caused by recent thrombosis of the superior mesenteric artery which must have developed postoperatively, since it was not seen at operation.

The cause of this patient's preoperative symptoms was unique in the experience of this laboratory — thrombosis of the celiac axis. The abdominal aorta showed severe arteriosclerosis, the intima being extensively frayed and fragmented. The orifice of the celiac axis was surrounded by a calcified plaque and the lumen was occluded by a gray adherent thrombus about 2 cm. long (Fig. 1). There was



FIGURE 1. Diagram of Abdominal Aorta and Its Branches. The shaded areas represent the older thromboses, whereas the black areas represent the more recent ones.

thrombosis of the hepatic artery and of its two branches well into the liver, with the result that the liver was extensively infarcted. What the surgeon removed was an early gangrenous gall bladder due to thrombosis of the cystic artery. The left gastric branch of the celiac axis was uninvolved. Two of the terminal branches of the splenic artery

ere thrombosed, probably by emboli from the iliac artery, with resultant infarcts of the spleen. The pancreas was not involved. Whether the cholecystectomy in some way started off this thrombosis I do not know, but I feel fairly sure that this occurred after the operation, because this thrombus was quite recent when compared with the thrombus in the celiac artery. Around the orifice of the superior mesenteric artery there was also an atherosclerotic plaque, which probably had something to do with the formation of this thrombus. There was no involvement of the renal or inferior mesenteric arteries.

Ordinarily one does not get such widespread infarction of the liver without damage not only to the hepatic artery but also to the portal vein. In this woman the portal vein was normal. These infarcts are similar to those produced experimentally by ligation of the hepatic artery, but there, of course, the occlusion is sudden. Here it probably was not so sudden. The presence of relatively old thrombi in the distal portions of the hepatic arteries and of a more recent thrombus in the proximal portion suggests that the hepatic occlusion began as emboli from the celiac artery. There were a few small emboli in the terminal vessels of the lungs.

DR. MAURICE FREMONT-SMITH: I wonder if the finding of extreme tenderness without spasm is helpful in making a diagnosis. I remember a patient at the Peter Bent Brigham Hospital, when I was a house officer there, who had extreme pain and tenderness but no spasm and who was found to have mesenteric thrombosis. Is the absence of spasm an important physical differentiation?

DR. McKITTRICK: I do not know.

DR. CASTLEMAN: I do not believe that this patient had mesenteric thrombosis when she came in. She had thrombosis of the celiac axis, and the pain was due to the gangrene of the gall bladder.

DR. FREMONT-SMITH: In other words, it was not inflammatory but circulatory. That is my point: there was not the amount of spasm that one would expect with an inflammatory process.

DR. SMITHWICK: Severe visceral pain may occur without spasm of the abdominal wall. If, for example, one blows up the small intestine with a balloon, thus creating intense, agonizing pain, the abdomen is flaccid.

DR. McKITTRICK: Spasm is an uncertain thing, particularly in old people. We see not a few patients with peritonitis who have no spasm. It is such a hard thing to evaluate that I cannot say how much she had, although she did have some.

DR. FRANCIS D. MOORE: One can have spasm over an infarcted loop of small bowel, once it has become gangrenous.

DR. McKITTRICK: But in such cases there is peritonitis. Whether spasm occurs before infection has set in, I do not know. It is a good point.

CASE 30512

PRESENTATION OF CASE

A seventy-year-old man was admitted to the hospital in coma.

The patient had apparently been well until the day before admission, when he developed pain in the left upper quadrant associated with nausea. Because of his condition no data concerning the character and radiation of the pain could be obtained, other than that it was apparently severe and constant. Several hours later, following an attempt at high colonic irrigation, the patient vomited black foul-smelling material. He was admitted to a community hospital and given morphine, following which he became stuporous and remained so. His skin was cold, and it was difficult to administer intravenous fluids. A white-cell count was said to have been 20,000. He was transferred to this hospital the following morning. For two or three weeks prior to admission he had been constipated.

The patient had had a cholecystectomy twenty-eight years previously, and an operation for a ruptured appendix two years later. Five years before entry he had had a prostatectomy, from which it took him nine months to recuperate. Both parents were said to have died of diabetes.

Physical examination revealed a well-developed and well-nourished comatose man. The pupils were contracted, and the tongue was dry. The skin of the extremities was moderately cold and clammy. There was tenderness in the left upper quadrant, where a firm, ill-defined, pulsating mass could be felt. Percussion over the area revealed dullness but no flatness. Peristaltic sounds were distinctly audible. Rectal examination revealed a depression in the region of the right lobe of the prostate, the remainder of the gland being firm but not enlarged.

The temperature was 101°F., the pulse 110, and the respirations 16. The blood pressure was 96 systolic, 80 diastolic.

A white-cell count was 13,400. The urine had a specific gravity of 1.020, with a +++ test for albumin, and the sediment contained many coarsely granular casts, 10 white cells and a rare red cell per high-power field; there was no sugar or diacetic acid. A blood sugar was 121 mg. per 100 cc. The serum nonprotein nitrogen was 43 mg., and the protein 7 gm. per 100 cc. The chloride was 98 milliequiv. per liter, and the carbon dioxide content 30.1 milliequiv.

A roentgenogram of the chest revealed only a high diaphragm bilaterally. X-ray examination of the abdomen showed gas in the stomach and colon,

but none in the small bowel. On the left side, near the transverse process of the third lumbar vertebra in the course of the ureter, there was a small ill-defined shadow of the density of calcium.

Catheterization on admission revealed only 5 cc. of urine in the bladder. A cystoscopy was performed, but no obstruction to the left ureter could be demonstrated, there being good urinary output from the kidney. Ten per cent dextrose in water, followed by 5 per cent dextrose saline solution, was administered intravenously. The pulse rate rose to 140, and the respirations to 30. The abdomen became tympanitic and diffusely tender, but peristalsis remained good. There was some flaccidity of the left leg, and the right corner of the mouth drooped, but no abnormal reflexes were obtained. The white-cell count rose to 17,700, and the non-protein nitrogen to 59 mg. per 100 cc. On the second hospital day the patient expired.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS D. MOORE: I should like to start off by looking at the x-ray films.

DR. GEORGE W. HOLMES: As already stated, the diaphragm is high on both sides, but the right half is definitely higher than the left. There is a great deal of gas in the stomach, but I do not believe that the colon is particularly dilated, although it is a little unusual that there should be so much gas there without any in the rectum. I suppose they thought that this area of calcification might have been a stone in the ureter. It does not look much like one. Since the ureter was catheterized, there is no reason to suspect that there was a stone.

DR. MOORE: Is the kidney abnormally displaced to the left?

DR. HOLMES: Yes; not only the kidney but also the ureter along its entire length.

DR. MOORE: Does this big area of "nothingness" suggest a mass that could be the one displacing the kidney?

DR. HOLMES: Yes; but I am not too certain about it.

DR. MOORE: We have here a seventy-year-old man who had pain in the left upper quadrant. I have gone over the record and tried to reconstruct the time relations. He was transferred to a local hospital, was given morphine and went into shock and coma all on the same day. The next day he came here, possibly with peritonitis, and the following day he died. Forty-eight hours transpired from the first acute symptom to death, with no operative procedure having been done. The pathologic process was a rapid one.

There are features in the record to suggest a great many diagnoses: gastric or colonic neoplasm, aortic aneurysm, ureteral stone, cardiac failure, chronic vascular nephritis, mesenteric thrombosis, cerebral thrombosis and benign hypertrophy of the prostate. I shall attempt to select the one

most responsible for his demise, although in all probability he had several diseases.

For three weeks prior to admission he had been constipated. Any man of seventy has a right to intermittent periods of constipation; however, since he was in coma and the history was obtained only from the family, they must have observed that he was having real trouble for three weeks. This suggests that the gastrointestinal tract was implicated. We find that after he received a colonic irrigation he vomited black foul-smelling material, which further suggests that he might well have had some sort of an obstructing lesion, even a gastrocolic fistula resulting from a neoplasm. But I am disturbed by the normal gas shadow in the stomach. The colon looks normal; there are no signs of tumor, and there is no abnormal distention. As a matter of fact I believe that is as good an air picture of that region as one could hope for. The patient had a tender mass in the left upper quadrant, which fits with the concept that he had a neoplasm in this region. He developed signs of peritonitis, compatible, of course, with a tumor that has ruptured or undergone necrosis. The white-cell count and temperature went up, which is also consistent with that general idea. There is no note of a guaiac test on a stool, which is unfortunate. One thing in the story is against gastrointestinal neoplasm; namely, at the time of admission to the hospital he was a well-developed and well-nourished man and one would not expect him to be such if he had a gastrointestinal neoplasm that had been there long enough to perforate, especially if a gastrocolic fistula had formed.

Renal tumor is possible, although the statement about the urine makes that unlikely; furthermore, the kidney was displaced in the wrong direction for a tumor of the parenchyma. The spleen or pancreas could have been involved, but it is hard to see how a tumor of the spleen or pancreas could produce death in forty-eight hours, even though it had undergone necrosis. Tumors of the pancreas associated with pancreatitis are, to my knowledge, rare.

How about aortic aneurysm? That seems like a good possibility. The mass pulsated. Incidentally, that does not make it an aneurysm because in an older person any mass that presses on large blood vessels pulsates. A big aneurysm at this point, big enough to be felt from the outside, would have to include a great many other vessels — the celiac axis, one or both mesenteric arteries and probably one or both of the renal arteries. So its formation would really be a disastrous event and could kill a person in a short time, as this lesion did. Against it, however, we have no previous history of heart disease or of hypertension, and the heart was not enlarged, according to the record. The facts that there was no calcification in the aorta and that the patient continued to have good urinary output are also against aneurysm.

The concept of ureteral stone is ruled out by the cystoscopic findings. I shall not spend further time on it.

How about the heart? It was not enlarged, but when he received 10 per cent dextrose in water and 5 per cent dextrose in saline solution, — it does not say how much or how fast, — the pulse went to 140 and the respirations to 30, which suggests that he did not have much cardiac reserve. Kidney damage is well substantiated by the record — albumin, casts, white cells, a rare red cell and a rising nonprotein nitrogen level; perhaps the last was due to dehydration, and yet in spite of the dehydration he could not concentrate over 1.020. So we are justified in saying that he had a chronic renal lesion. The fact that he had only 5 cc. of urine in the bladder was perhaps due to shock.

A cerebral vascular accident seems likely because he went into coma rapidly. One might ask, Could the coma have been due to the morphine? It is worth while pointing out that when he came to this hospital he was still in coma but the respirations were 16; hence, morphine poisoning seems unlikely. Since he had a flaccid left leg and something wrong with the mouth, he probably had had a cerebral vascular accident. Venous mesenteric thrombosis can be rapidly fatal and can at times produce a mass, but the mass is due to the matted loops of gangrenous bowel and I should not expect that it would transmit pulsation from the aorta.

Pulmonary embolism is also possible, but it may have been masked by other things.

I have mentioned all the pathologic processes that are suggested by the record. There are points pro and con on all of them, but I am going to take as my first diagnosis a malignant lesion of the gastrointestinal tract, either in the stomach or large bowel, I do not know which, with local rupture producing peritonitis and shock. I hypothecate that he was given morphine while in shock, that this further depressed his activity and possibly lowered his blood pressure and that he then developed a cerebral thrombosis, which produced neurologic signs. I believe that he also had arteriosclerotic heart disease, chronic vascular nephritis and probably benign hypertrophy of the prostate. As a second choice, I shall say aortic aneurysm.

I should like to ask Dr. Holmes, now that I have made my diagnosis, what his x-ray diagnosis would be purely on the basis of the displaced kidney.

DR. HOLMES: There is just a possibility that that was simply technical because of the way the film was taken. If the kidney is displaced one would have to think of a retroperitoneal mass. I should not expect a ruptured viscus to do that unless there was an abscess behind it.

DR. MOORE: Would you expect an aortic aneurysm to do it?

DR. HOLMES: That is a possibility, but I should think that an aneurysm capable of doing that would also have eroded the bodies of the vertebrae, provided that it had been there any length of time.

DR. MOORE: And also completely destroy the renal vessels, which it did not do.

DR. HOLMES: It might be a retroperitoneal mass of some sort, but I cannot go any farther.

DR. MAURICE FREMONT-SMITH: This was an extremely interesting case. Additional history was obtained afterward. For three months before entry this man had had pain in his back, for which he had gone to an osteopath several times for treatment, with apparent improvement. Both dorsalis pedis arteries were palpable and pulsating. Anuria was a striking part of the picture. Although Dr. Colby reported that the kidneys were excreting urine, we catheterized him twice without obtaining any. The mass was definitely pulsating. We wondered if it was a mass lying over the aorta, in spite of the fact that it was well out to the left.

DR. MOORE: Was it expansile?

DR. FREMONT-SMITH: I cannot say, but it had a definite pulsation. We thought that he had had a vascular accident, but the pulsating dorsalis pedis arteries argued against a dissecting aneurysm. Our tentative diagnosis was a rupture of an aneurysm of the renal artery, with a retroperitoneal mass of blood connected with a vessel. We also thought of the possibility of a cerebral accident, but did not believe that it could have been the cause of death.

DR. BENJAMIN CASTLEMAN: Dr. Moore, have you anything more to say?

DR. MOORE: These points certainly make me incline toward aneurysm more than anything else.

CLINICAL DIAGNOSES

Aneurysm of left renal artery, with rupture into retroperitoneal space?
Cerebral thrombosis.

DR. MOORE'S DIAGNOSES

Gastrointestinal neoplasm, with rupture and peritonitis?
Aortic aneurysm, with rupture?
Arteriosclerotic heart disease.
Chronic vascular nephritis.

ANATOMICAL DIAGNOSES

Aneurysm of abdominal aorta, with rupture into left retroperitoneal space.
Arteriosclerosis, generalized.
Cardiac hypertrophy, hypertensive type.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed a large retroperitoneal mass, which proved to be a hema-

toma, measuring 22 by 14 by 10 cm., that surrounded the left kidney, adrenal gland, renal artery and ureter and was surmounted by the spleen and pancreas. The hematoma had resulted from a rupture of an aortic aneurysm beginning below the level of the renal arteries and extending to the bifurcation.

DR. MOORE: Where was the kidney in relation to the mass?

DR. CASTLEMAN: Completely surrounded by the hematoma.

DR. MOORE: Was its circulation obliterated?

DR. CASTLEMAN: No; the aneurysm occurred below the level of the renal artery. The hematoma

surrounded the kidney and renal artery, but the artery was not intrinsically involved. The anuria was probably due to shock. There was slight vascular disease of the kidney.

DR. HOLMES: It is unfortunate that we did not have better films of the kidney. I suppose the patient's condition was too poor.

DR. MOORE: Was anything found in the brain?

DR. CASTLEMAN: It has not been sectioned yet. Small multiple thrombi will probably be found to account for the symptoms.

DR. HOLMES: Were the vertebrae involved?

DR. CASTLEMAN: No.

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CHRISTMAS, 1944

CHRISTMAS this year, as never before, will be celebrated by Americans in many lands and in strange anners. In improvised hospitals from Alaska to India and from New Zealand to the fields of Flinders, American doctors and nurses will be bringing the traditional cheer of the season to many thousands of their sick and wounded countrymen. The hard-pressed islands of the Pacific will feel its temporary impact, and it will be briefly acknowledged in the stubbornly defended mountains of northern Italy and in the rutted mud of western Europe.

December 25, in short, is Christmas, and it will evoke the same images, nostalgically, and have the same meaning to millions of modern crusaders upon

whom the sun now never sets as it will in their homes in Massachusetts or in California or in Montana.

We have a right, we hope, to believe that this Christmas is witnessing the peak of our foreign military traffic; that before another season of giving has come around, we will have ceased to include among our overseas packages those of reeking tubes and iron shards; that our hard-pressed enemies will have decided to cry "Enough," and will embrace once more — or for the first time — the doctrines of peace on earth and of good will toward other men.

Our victory is in sight, but it is at the end of a long road that is still not too close to its ending. We can be thankful that we are approaching that end, however, in the company of a good fellowship, all bent on the same goal and with the same motives. It is as Paul, approaching Rome in some tribulation, found that the brethren had come to meet him, even as far as Appii Forum: "Whom, when Paul saw, he thanked God, and took courage."

Christmas provides as good a motive for referring to the Scriptures as any, if a motive need be sought, so let us add one more singularly appropriate quotation, from the best loved Psalm: "Thou preparest a table before me in the presence of mine enemies: . . . my cup runneth over."

PROPHYLACTIC USE OF SULFONAMIDES

THE herding and alteration in the mode of living of young adults in time of war inevitably result in epidemics of viral and bacterial disease, especially infections of the upper respiratory tract. The present war has been no exception, although there have been striking differences in its epidemic diseases from those of World War I. Fatalities and serious illnesses have been greatly diminished as the result of new therapeutic agents, but the loss of manpower days as the result of upper respiratory infection has been and continues to be a serious military problem.

Reports of Group A hemolytic streptococcus epidemics among military populations are now appearing in the medical literature. Not only have there been large numbers of cases, but also the frequency of associated rheumatic fever makes this problem one of great importance to the services,

especially in the training of military personnel. The latter causes long periods of illness, and those who are so afflicted must either be discharged from the services or run the danger of repetitive or recurrent disease.

It is natural that the armed services have developed prevention programs for the curtailment of hemolytic streptococcus infections and rheumatic fever. The reports to date largely concern the administration of small daily doses of sulfadiazine to large numbers of personnel. Holbrook,¹ Coburn² and Keith³ have recently reported such studies. These papers offer interesting material and data that require much thought and even philosophical speculation. All three authors agree that such sulfonamide prophylaxis sharply decreased the volume of streptococcal disease in the respective populations. In one instance it was indicated that the incidence of rheumatic fever was reduced, parallel to that of streptococcal diseases, and in another this mass prophylaxis was reported as effective in preventing the development of disabling sequelae caused by these bacteria.

A further report on sulfonamide prophylaxis in the armed forces appears elsewhere in this issue of the *Journal*. In keeping with the previous reports, Dr. Hodges reports a diminution of bacterial disease, especially streptococcal infections, as well as rheumatic fever, in the treated groups. Attention should be particularly directed to one of the figures of his report, which shows a continued rise in the streptococcal infections in the control group coincident with a sharp fall in these infections in the treated group. This appears to be the most convincing information yet published.

These reports are of broad significance and importance. The data as yet available, however, do not permit accurate appraisal of the results. Variations in susceptibility, length of military experience, the composition of individual units, the length of service in a given station, housing and so forth make such disease-control measures a complex problem, the evaluation of which is fraught with difficulty. There can be little doubt that more than suggestive evidence of the immediate success of sulfonamide prophylaxis is presented. Eventual analyses with more detailed information may indicate that factors other

than the drug prophylaxis were at least partially responsible for the results obtained.

A recent editorial in the *Journal* discussed the dangers of continuous sulfonamide therapy.⁴ The development of sensitization to the sulfonamides and the creation of drug-resistant strains of bacteria were stressed as possible deterrents in this type of prophylactic control. Several new developments suggest the pertinence of these previous remarks, and it seems advisable to re-emphasize some of the possible and inherent dangers of such mass prevention studies.

Little can be added concerning the development of sensitivity or toxic reactions to the drug. Reports continue to indicate that such cases are rare. The report of French and Weller,⁵ however, needs emphasis. Fatalities as the result of myocardial changes following therapeutic doses of sulfonamides are apparently increasing, and one can only wonder what will develop in young men who have received small prophylactic doses of sulfonamides when they are given large therapeutic doses at a later period. The future alone will give the complete picture.

The question of drug-resistant strains seems more immediately pertinent. Hendry⁶ has demonstrated the development of drug-resistance by a Group A hemolytic streptococcus. Since virulence or pathogenicity seems unrelated to drug-fastness, the possibility of the development of epidemics with drug-fast strains seems entirely tenable. Indeed, Wright, Cruickshank and Gunn⁷ have reported their inability to control the spread of a drug-resistant Group A (Type 6) hemolytic streptococcus in a measles ward by sulfonamide prophylaxis. The ease with which strains may become drug-resistant remains to be determined, as well as many other puzzling features. It seems not unlikely that the widespread therapeutic and prophylactic use of sulfonamides will eventually produce many resistant strains and that penicillin will prove to be as necessary in these as in gonococcal infections.

Another feature of such prevention programs remains unexplored. Little is known concerning what role long-continued sulfonamide prophylaxis plays in the development of antistreptococcus immunity. It is possible that protection at one time results in a continuation of susceptibility and the develop-

ment of appreciable patterns of illness on later exposure to infection. Some information concerning this may be available in the future.

Military necessity will, of course, dictate the continuation of sulfonamide prophylaxis. Even in such populations the alleviation of an immediate problem may ultimately prove to effect adversely the future health of service personnel. So far as civilian populations are concerned, there seems little justification for the wholesale and uncontrolled use of long-continued sulfonamides, save on a purely experimental basis, with a carefully thought-out and controlled study. Furthermore, attention should be directed to other measures for the control of streptococcal infections that are not accompanied by the dangers and difficulties mentioned above. Dust control (by the oiling of floors and bedclothes), sterilization of the air by ultraviolet irradiation and the use of aerosols, ventilation, improved methods of housing and so forth may be mentioned as procedures of probable benefit.

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BARONE — Anthony Barone, M.D., of Boston, died December 8. He was in his forty-ninth year.

Dr. Barone received his degree from Tufts College Medical School in 1917. He was also a dentist and registered pharmacist. He was a member of the American Medical Association and the Massachusetts Dental Society.

His widow, four daughters, five brothers and two sisters survive.

GODDARD — Frederick C. Goddard, M.D., of Uxbridge, died November 7. He was in his fifty-second year.

Dr. Goddard received his degree from Tufts College Medical School in 1917. He enlisted in the army immediately following his internship at St. Elizabeth's Hospital. For the past twelve years he has been a member of the visiting staff of Milford Hospital. He was a member of the American Medical Association and a past president of Thurber Medical Association.

His widow, two sons and a daughter survive.

KELEHER — William H. Keleher, M.D., of Woburn, died December 4. He was in his seventy-sixth year.

Dr. Keleher received his degree from Harvard Medical School in 1892. He was a director of Choate Memorial Hospital and a former medical examiner of the Fourth Middlesex District. He was a member of the American Medical Association, and was president of the Middlesex East District Medical Society in 1913.

His widow, four sons, a daughter and a sister survive.

LEHNHERR — Earl R. Lehnher, M.D., of Brookline, died December 4. He was in his forty-second year.

Dr. Lehnher received his degree from Harvard Medical School in 1931. He was a staff member at the New England Deaconess Hospital and the Palmer Memorial Hospital and was associated with the Allergy Clinic of the Massachusetts General Hospital. He was a member of the American Medical Association.

His widow and a son survive.

PERKINS — Roy S. Perkins, M.D., of Lowell, died December 3. He was in his fifty-fifth year.

Dr. Perkins received his degree from Bowdoin Medical School, Brunswick, Portland, in 1914. After practicing for two years in Lowell, he entered army service in 1917 and served overseas for 14 months as a captain in the Medical Corps. He conducted an x-ray laboratory in Boston and served as radiologist at St. John's and St. Joseph's hospitals in Lowell, at the Peabody and Salem hospitals and at the Massachusetts State Hospital in Tewksbury. He was president of the staff of St. John's Hospital and a past president of the staff of St. Joseph's. He was a fellow of the American X-ray Society and a member of the American Medical Association.

His widow, a sister and a brother survive.

SCARITO — Nicholas J. Scarito, M.D., of Lawrence, died December 3. He was in his sixty-sixth year.

Dr. Scarito received his degree from George Washington University School of Medicine in 1912. He was a member of the American Medical Association.

His widow, a son, a daughter, a grandchild and two brothers survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

VISION TESTING IN MASSACHUSETTS SCHOOL CHILDREN

Eye tests for school children are a major concern of school health departments, particularly of the school physicians. Since poor eyesight is often remediable, no child should be permitted to struggle through school for lack of attention to a visual deficiency. An ophthalmologic examination for every school child would be ideal, but since practical considerations make such a program impossible, parents, nurses and teachers can be enlisted to serve as reconnaissance groups for discovering children with visual defects. The school seems to be the agency best suited for directing a large-scale reconnaissance project of this kind.

Although lay persons ordinarily should not be expected to make diagnoses or suggest treatment, most teachers and nurses can become highly skillful in administering subjective tests and obtaining reliable test responses. By careful observation for symptoms, supplemented by a comprehensive

screening test, the school staff is in a position to detect the majority of children needing the attention of the eye specialist.

Such a test is the new "Massachusetts vision test," already serving about a third of the towns in the Commonwealth. It was designed particularly with a view toward getting a better job done in the schools and to stimulate attention to the related problem of sight conservation. It is particularly notable for the precise instructions provided for those giving the test, as care and exactness are essential in order to get good results. Since persons with special interest and aptitude in giving such tests usually obtain superior results with less expenditure of time and effort than those who labor over such work without enthusiasm, it is suggested that persons with these special aptitudes be selected for performing the tests. Whether the tester be a teacher or a nurse, she should be chosen because she excels in the easy handling of children, has a quick grasp of essential details and uses good judgment in recording a child's responses.

This new test includes a Snellen chart employing the symbol E (with the middle prong the same length as the other two), which is considered superior to the numbers or letters commonly used on vision test cards. The card is to be read at a distance of 20 feet. Illumination is standardized by means of an electric bulb arranged to give an even distribution of approximately 15 foot candles over the surface of the chart. According to the Snellen formula, the "20 line" is the critical test. Failure to read this line correctly at the 20-foot distance is interpreted as a deviation from normal, and the child who cannot read this line with either eye is therefore referred for a retest. Failing this, he is then referred to the family specialist for examination. About 90 per cent of all children picked up by the school test are found by the simple use of this modified Snellen card.

Two other checks are included in the test: one for latent hypermetropia, which employs plus (+) spherical lenses in eyeglass frames, and the other, a check of muscle imbalance. The latter makes use of a multiple Maddox rod mounted for the right eye in a spectacle frame, with no lens for the left eye. The object of fixation is a small light arranged in a simple device for describing the degree of heterophoria. These two tests are so easy for a lay person to administer that only a minute or two is required for each child. There is some controversy over the practicability of these additional tests, because some ophthalmologists refuse to correct moderate degrees of hypermetropia in children and some decline to prescribe for muscle imbalance. Experience with large numbers of cases, however, presents evidence that correction, often temporary, is often highly beneficial, especially for children with records of poor school achievement.

The test is receiving high praise from specialists who are examining school children selected by the method. Of particular interest to some of them is the fact that certain children, hitherto not detected, yet suffering from eyestrain, are being discovered, particularly those with latent hypermetropia.

MISCELLANY

GRANTS BY THE BARUCH COMMITTEE ON PHYSICAL MEDICINE

The Administrative Board of the Baruch Committee on Physical Medicine has announced the granting of an additional total sum of \$185,000, which is being given by Mr. Bernard M. Baruch for the further advancement of the program in physical medicine and the physical rehabilitation of those disabled in the war. This sum has been divided into seven grants as follows: \$50,000 to the Massachusetts Institute of Technology; \$40,000 to the University of Minnesota Medical School; \$30,000 to the Harvard Medical School; \$30,000 to the University of Southern California School of Medicine; \$15,000 to the State University of Iowa College of Medicine; \$15,000 to the University of Illinois College of Medicine; and \$5000 to the Marquette University School of Medicine.

The grants to the Massachusetts Institute of Technology and the University of Minnesota are in addition to the gift of \$1,100,000 made by Mr. Baruch in April, 1944, at which time grants were made to Columbia University College of Physicians and Surgeons, New York University College of Medicine, the Medical College of Virginia and for minor research and fellowship programs for the advancement of physical medicine.

The present gift to the Massachusetts Institute of Technology is in support of a five-year program of training and research in electronics, instrumentation and physics in relation to medicine, to be carried on under the auspices of the Department of Biology and Biological Engineering. It was the conviction of the Scientific Advisory Committee of the Baruch Committee on Physical Medicine that Baruch fellows and other physicians should have more than a superficial knowledge of the physics and technology underlying the physical methods and instrumentation used in this field, and it was suggested that training in this aspect might effectively be centered at the Massachusetts Institute of Technology. The program will be under the general supervision of Francis O. Schmitt, head of the Department of Biology and Biological Engineering and under immediate supervision of K. S. Lion, assistant professor of applied biophysics, who is an expert in physical instrumentation.

The other grants have been allocated from the fund of \$200,000 given by Mr. Baruch in April. The sum of \$30,000 was granted to Harvard Medical School for the establishment of a three-year program to provide fellowship or residencies to be used for the benefit of qualified physicians who are selected to be trained in this field. This sum will be administered by the Standing Committee on Physical Medicine, recently appointed by Dean C. Sidney Burwell of Harvard Medical School, composed of Drs. J. B. Ayer, D. Denny-Brown, W. T. Green, J. H. Means, A. L. Watkins and E. M. Landis (chairman). Appointments to the fellowships, which generally carry stipends of \$2500 or \$3000, will be made annually but may be renewed to provide up to three years of specialized study and research. Emphasis will be placed on training a few men in basic research and clinical investigation.

Unusual opportunities for clinical experience and research in the psychologic and psychiatric aspects of physical medicine will be available at Harvard. The first year will be wholly or in part devoted to basic research related to physical medicine in one of the preclinical sciences, such as physiology, anatomy or biophysics. The second year will be spent in clinical training in physical medicine at the Massachusetts General Hospital and other hospitals affiliated with the Harvard Medical School. In the third year, fellows will be

assistants in physical medicine with clinical responsibilities. For candidates with extensive previous training, one-year clinical fellowships will also be granted. Applicants must have an M.D. degree from an approved medical school and a minimum of one year of internship in an approved hospital.

PULMONARY TUBERCULOSIS AS INFLUENCED BY WARTIME RELOCATION

The danger that an unsuspected case of tuberculosis will infect others is present wherever human beings live in close contact. Whether it be in families, in schools, in offices, or under such artificial conditions as were produced by the evacuation of children from the danger areas in England is not important—the significant factor is always the case which is not recognized until too late to prevent spread of the disease. Too often children are overlooked in the search for contacts when a case of tuberculosis is discovered. The following abstract from a recent paper (Hall, M. Pulmonary tubercle in children: influence of evacuation on its incidence. *Lancet* 2:35-37, 1943) discusses the problem.

* * *

An increase in tuberculosis in England following the outbreak of the war seemed to justify collection and examination of the results of work among tuberculous children in East Sussex in relation to the spread of the disease traceable to evacuation and billeting.

Little work has been done in England on locating the source of tuberculosis observed among children. Reports from Scandinavian and American investigators show that wherever the background of these children is carefully studied, large numbers of unsuspected spreaders of bacilli can be detected among their contacts, since infection quickly registers among children exposed to open cases of tuberculosis. This has been demonstrated by our experience with evacuated children.

History, physical examination, tuberculin skin tests, blood sedimentation rates and chest x-ray films were recorded in all cases. Gastric lavage was done on cases admitted to the hospital.

Cases showing the effect of billeting healthy children with others who have open tuberculosis are as follows:

Case 1. A girl twelve years old was admitted to the hospital with a diagnosis of rheumatism. She was found to have a cough of several months' duration but previous examinations made in London had proved negative for tuberculosis. Therefore, the tuberculosis office of the reception area had not been notified. Cavities were found at both apices. This was confirmed by x-ray. The blood sedimentation rate was 21 mm., later being 50 mm.; the sputum was loaded with tubercle bacilli.

School contacts. Four children out of 15 were found to be infected with tuberculosis. Two others showed suspicious x-ray findings. All children were re-examined at three-month intervals until calcification developed in the primary foci and mediastinal nodes.

Billet contacts. A girl six years old was infected by Case 1, who was billeted with the parents of Case 2 for six months, during which time the child developed a cough. She had a pleural effusion in the right base, demonstrated by x-ray. The primary complex appeared as this cleared. The child made a good recovery, with healed calcified lesions in the right lung appearing later.

Another contact was an eight-year-old girl who was admitted to the hospital complaining of abdominal pain. She gradually developed tuberculous meningitis and died after three weeks. X-ray films showed miliary tuberculosis. She spent a month with Case 1 at a holiday camp, sharing a bed with her at this time.

Case 2. A boy eleven years old was sent to the local practitioner because he looked thin. The doctor found suspicious signs in his chest and sent him to the hospital. The school medical officer had examined this boy with special attention because his mother had died of tuberculosis but did not x-ray his chest. No note had been sent to the tuberculosis officer of the reception area. There were cavities at both apices, confirmed by physical signs. Gastric lavage showed many tubercle bacilli. In addition to the boy's mother, a brother and a sister in the same

family died with tuberculosis and the child himself had attended a tuberculosis clinic.

School contacts. In all, 40 children and their teacher were examined; 11 of them were found to have been infected with tuberculosis; 6 of these showed definite activity, 4 had healing lesions and 1 had a calcified lesion.

Billet contacts. Case 2 was billeted with 5 other children, 3 of whom became infected with tuberculosis. One child in this group had sanatorium treatment.

The effect of billeting healthy children in households in which there is or has been tuberculosis is no less serious, as is illustrated by the case of a child of five who entered the hospital with phlyctenular conjunctivitis and was found to be infected with tuberculosis. She was one of six brothers and sisters, all previously healthy, who were placed with a foster-mother known to have had tuberculosis eight years previously. This woman had a bad cough while the children were living with her but refused examination. Four of the six children were found to have tuberculosis.

Neglecting the examination of child contacts may also have disastrous results, as is shown by the following case:

Case 3. A girl six years old died in the hospital of miliary tuberculosis. The child was infected by her aunt, a young adult who had entered a sanatorium some months before. The child had often visited her but had not been examined, and the tuberculosis officer in the reception area had not been notified.

School contacts. Case 3 attended an evacuation school and all the children, 39 in number, and 3 teachers were examined. Eight children had evidence of recent tuberculous infection.

Two of the children examined with this school were also found to have tuberculosis. The infection in the case of these two was traced to their mother, who had died from tuberculosis four months earlier. After the death of the mother one child had been examined clinically but no x-ray films were taken.

Billet contacts. A brother and a cousin, the latter of whom died of tuberculous meningitis, were found to be infected. Another brother remained healthy.

In reviewing these cases one is impressed by the importance of the search for child contacts and the little attention usually paid to them. So great is the risk of bacillary transmission that all children who have been in close or repeated contact with a case of reinfection pulmonary tuberculosis should be regarded as having become infected until it is proved otherwise.

To be domiciled with a case of open phthisis is relatively much more dangerous than to attend the same school with a case. Physical examination that deals with the exterior of the chest alone is worthless in children and may be dangerous, as an infected child may be labeled as "normal." All child contacts should have complete examinations, including tuberculin tests and x-ray examinations.

Wherever children are placed in a new environment, great care should be taken to establish that they are not suffering from tuberculosis and that they are not thrown unwittingly into contact with it. Certainly, a more intensive search must be made for all child contacts of open cases of tuberculosis. — Reprinted, with changes, from *Tuberculosis Abstracts* (December, 1944).

ELLA SACHS PLOTZ FOUNDATION

During the twenty-first year of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation, twenty-seven applications for grants were received by the trustees, nineteen of which came from the United States, the other eight coming from five different countries in Europe, Asia and South America.

In the twenty-one years of its existence the Foundation has made five hundred and eight grants which have been distributed to scientists throughout the world.

In their first statement regarding the purposes for which the fund would be used, the trustees expressed themselves as follows:

For the present, researches will be favored that are directed toward the solution of problems in medicine and surgery or in branches of science bearing on medicine and surgery.

As a rule, preference will be given to researches on a single problem or on closely allied problems; it is hoped that investigators in this and in other countries may be found, whose work on similar or related problems may be assisted so that more rapid progress may be made possible.

Grants may be used for the purchase of apparatus and supplies that are needed for special investigations, and for the payment of unusual expenses incident to such investigations, including technical assistance, but not for providing apparatus or materials which are ordinarily a part of laboratory equipment. Stipends for the support of investigators will be granted only under exceptional circumstances.

In the past few years the policy outlined in the second paragraph has been neglected and grants will be given in the sciences closely related to medicine without reference to special fields. The maximum size of grants will usually be less than \$500.

Applications for grants to be held during the year 1945-1946 must be in the hands of the Executive Committee before April, 1945. There are no formal application blanks, but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. In their requests for aid, applicants should state whether or not they have approached other foundations for financial assistance. It is highly desirable to include letters of recommendation from the directors of the departments in which the work is to be done. Only applications complying with the above conditions will be considered.

Applications should be sent to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston 14.

CORRESPONDENCE

FUTURE OF MEDICINE

To the Editor: The article "Justice and the Future of Medicine" by Wendell Berge, published in the November 30 issue of the *Journal*, is a thought-provoking presentation of the problem of social medicine that should be read and pondered by every doctor.

Good health is both an individual and a community asset. The prosperity of a community may, with reason, be said to depend on its health.

Medical knowledge regarding preventive, diagnostic and curative procedures has ranged far ahead of the application of this knowledge. With the improvement of medical procedures the cost has increased.

Within limits, both private and public health can be purchased, provided the cost of applying known medical measures can be met. Medical economics is the study of how to obtain the best medical care and protection for the greatest number of people at the lowest possible cost and in the most satisfactory manner. In spite of the great accomplishments of medicine it cannot be denied that the people want something more.

Mr. Berge suggests: "If an instrument of common health can be provided on terms the people can afford the people will rejoice. If you do not help them to it the people will seize whatever agencies are at hand as a help in need. For the universal demand that the common health be served cannot much longer be delayed."

If there is a lesson to be learned from Mr. Berge's article, — and I think there is, — it is that doctors should play a leading part in shaping this "instrument of health" and in the development of all medical measures; they should not only insist on the provision of the highest quality of medical care but also guide in other ways. Scientific advancement is always needed, but practical and universal application of these advances are equally important.

A sound health program must be founded on sound basic principles and policies. As a constructive addition to the study of this vital problem of medical economics, I enclose a summary of "Principles of a Nation-Wide Health Program," which is a detailed report prepared by the Health Program Conference. Every doctor should read the full

report carefully and without prejudice and then consider what he, personally, should do about it.

NATHANIEL W. FAXON, MD

Massachusetts General Hospital
Fruit Street
Boston 14

* * *

PRINCIPLES OF A NATION-WIDE HEALTH PROGRAM*

This program and these principles are the joint product of twenty-nine men and women of differing interests: thirteen physicians, some in private practice and others in universities, health agencies and hospital administration; six economists, a majority of whom have long studied and worked for health insurance; the research directors of the American Federation of Labor and the Congress of Industrial Organizations; and eight administrators connected with voluntary or governmental agencies. The problems of dentistry, nursing and pharmacy have not thus far been considered.

Under the program that the Conference proposes, the medical services would be comprehensive. Plans of medical care of a community that are limited to hospitalization, surgery or "catastrophic illness" are helpful and should be encouraged, but they cover only a part of the medical needs. Plans that provide only cash payments to meet the cost of services, in whole or part, are not desirable because such cash payments may be used for other purposes. Only comprehensive preventive, diagnostic and curative service will minimize disability, inefficiency and premature death, which bring heavy losses not only to individuals but to productive industry and agriculture.

The program should cover all or most of the population. In the opinion of the Conference, limitation of coverage to certain income groups or to those engaged in certain occupations would not be satisfactory. Those who wish to purchase medical care outside of the national health system should be free to do so.

In order that comprehensive service shall be available to all or most of the population and in order to minimize the administrative costs of acquiring members, it is essential that financial participation in the system be compulsory, provided that, as we have said, those who wish to purchase comparable medical care outside of and in place of a national health system should be free to do so. American families ordinarily spend directly about 4 per cent of their earnings for all kinds of medical services. Of this, the expenditures for physicians and for hospital services constitute about three fourths, that is, about 3 per cent of the annual income. The American people are now spending for physicians' services and hospitalization enough to make it possible to provide adequate medical care for all, with only minor supplementation.

The insurance principle applied to medical expenditures will mean no greater expenditure of money but should result in better medical care, regularizing existing payments rather than imposing new burdens. The expense of physicians' and hospital services would be met by a national system of contributory health insurance, supplemented by taxation. We recognize that there must be a certain amount of federal direction, but administration must be decentralized on a state basis, recognizing voluntary as well as governmental agencies. The quality of care and the status of the medical profession should be fostered by improved professional organization of service, by retaining the freedom-of-choice principle, and by adequate compensation and educational opportunities.

The amounts of payment from employees and self-employed persons should be related to the earnings of the contributors. It is generally considered that it is desirable that employers should also contribute. Because of the inadequate provision of hospitals and other medical facilities in some parts of the country, particularly in rural areas, capital funds for such facilities are necessary "which, insofar as unavailable from nongovernmental sources, should be provided by federal, state or local taxation, or combinations of these."

The national health program should include general tax funds from the start, especially to aid in the construction

*A summary of a report published for the Health Program Conference by the Committee on Research in Medical Economics, 1790 Broadway, New York 19, New York.

and operation of new or improved hospitals or health centers, particularly in rural areas, in the further extension of full-time public-health departments, in the application of preventive measures made available in every part of the country and in the provision or improvement of medical services to those dependent on and other persons not directly covered by the insurance system.

The report is not a draft of legislation. It sets forth policies and principles, including those of organization, and does not specify the governmental agencies to be involved. Participation between the profession and the public is emphasized throughout. The people cannot obtain a high quality of service unless adequate training, intellectual freedom and economic security are assured to physicians.

The national policy-determining body for the administration of a health program must be composed of representatives of the chief groups of those who receive service and of those who furnish it. Similar policy-determining bodies should be organized at local and intermediate levels. All policy-determining bodies should be responsible to the interest of the general public, as distinguished from the interest of any vocational or economic group.

The administrative officers working under such public bodies should be removed as fully as possible from partisan political pressures and should fall into two operating groups: professional and financial. The strictly medical activities should be under qualified members of the profession. Financial responsibilities should be placed under the control of a financial group. Both the professional and financial officials, each having administrative authority in their respective fields, would be co-ordinated through the policy-determining body. Thus, when the decisions had to do with medical considerations only, they would be made by the medical administrators aided by advisory councils of physicians. When decisions related to general policies they would be made by a joint group representing both the profession and the public. These principles would apply to each local area, as well as on national and intermediate levels.

The administration of services should be decentralized, with "responsible participation of local physicians and agencies (governmental and voluntary) in the administration and control of their health services under national standards; the funds and administrative agencies of local subdivisions and of the states might well be utilized in planning and in the provision of services." The local organization "should be the administrative unit and the foundation of the national system."

Voluntary hospitals with their extensive facilities would continue under the system, maintaining their autonomy; and voluntary health-insurance plans would also be recognized. "Voluntary agencies providing services of acceptable standard should have the right to participate in the system. Voluntary agencies not providing services should have the right to participate if they contribute to the efficiency and economy of the system. Under these principles, voluntary agencies which directly provide physicians' services or hospitalization of acceptable standards would be eligible to participate in the system, but agencies would not necessarily be included when they were concerned only with the collection of funds and the distribution of cash indemnities to beneficiaries."

In order to maintain and improve the quality of service, the career of a physician must offer stimulating professional opportunities and adequate financial compensation. There must be ample support for medical education and research: freedom of experimentation in medical science, medical technology and in the different types of medical practice. Group medical practice is to be encouraged. The organized staffs of the best hospitals and clinics now constitute the most widely diffused examples of group medical practice. Unfortunately, the advantages of group practice in these hospitals are at present not universally achieved for all classes of patients, often being limited to those in the low income brackets, the so-called "ward patients." Hospitals and clinics should be reorganized, as some of them have already been, so that comprehensive service through group medical practice will become available to people of all incomes. As medical centers, it is possible that hospitals may ultimately provide preventive, diagnostic and therapeutic services for bed, ambulatory and home patients, and also office facilities for the physicians on their staffs.

In the full report, certain principles regarding the payment of physicians are stated. "Compensation should be adequate." The other principles relate to judging adequacy of income and to fixing the best method of payment under various circumstances. Fee-for-service payment has been the long-accepted method of payment in spite of certain disadvantages. Alternative principles stated in the report would permit fees for service, but "would tend to encourage the compensation of general practitioners by the capitation or the salary method."

How would the method of payment be decided? In each local area the general practitioners carrying on private practice would determine by majority vote the method of payment that they preferred, but "those physicians who wished to carry on group instead of individual practice in the same area, and to be remunerated accordingly, would also be protected in their right to do so." Specialists, qualified under standards set by professional bodies, would be paid on a fee or a salary basis according to local arrangement. The incomes of hospitals under a nation-wide health program would be mainly derived from services rendered to beneficiaries of the program. Consequently, payments from the health-insurance fund to the hospitals must be adequate to support high-quality service. Here and elsewhere, the full report develops many of the items in more detail.

The basic "principles of freedom" for the people and for physicians must be assured. People "should be entitled to choice among individual physicians, organized groups of physicians, hospitals, clinics and any other agents, agencies or service recognized under the law; and also to change their sources of service when they so desire, under reasonable regulations." Physicians, on their part, should have "the right to accept or reject patients; the right to participate or not to participate in a publicly established system; the right to be represented in negotiations through organizations of their own choosing; and the right to furnish services as individuals, or to organize medical groups, or to associate themselves with existing medical groups or hospitals which will accept them."

The program based on these and the preceding principles was developed by the Conference in "the belief that there is now need for public action to make adequate medical care more widely accessible to the American people and to improve the quality, organization and economy of medical services."

BOOK REVIEWS

To the Editor: Is there something wrong with the Book Review Section of the *Journal*? We admit this is rather a bold question but nevertheless a serious one.

At the beginning of 1943 a book *The Inner Ear* by Joseph Fischer and Louis E. Wolfson was sent to many leading medical journals, including the *New England Journal of Medicine*, *Journal of the American Medical Association*, *Archives of Otolaryngology*, *Annals of Otolaryngology*, *Laryngoscope*, *War Medicine*, *Lancet* and so forth. Without exception the reviews were highly favorable, and the general trend of comment was that the book filled a long-felt want. All the journals, with the exception of the *New England Journal of Medicine*, published their reviews of this book promptly and more than one year ago. The book review in the *New England Journal of Medicine* was published in the October 12, 1944, issue, more than one year after all the other reviews had appeared. This review commented only on the first two chapters and was most unfavorable. The statement was also made that in the coming second edition (about which the authors have no knowledge) the reviewer expected improvement.

We believe that the editors of the Book Review Section of the *Journal* could well re-read, with profit, the letter of Dr. Frank H. Lahey in the *Journal* of November 4, 1943, in which he particularly emphasized the desirability that the reviewer be a qualified critic and that his criticism should not be colored by personal prejudice. The letter of Dr. Henry A. Christian in the *Journal* of March 2, 1944, is also pertinent in that he gives some very good reasons in favor of signed book reviews.

*Further study should be given to a supplementary method of payment for the minority other than that determined by the majority.

Surely there must be something wrong when the *New England Journal of Medicine* reviews a book more than a year after all the other medical journals mentioned above, all of them having received the book at the same time. The complete lack of agreement of the *Journal's* review with those of the other periodicals can of course not be commented upon, but it raises questions as to the correctness of the reviewer's opinions as expressed in the *New England Journal of Medicine*.

LOUIS E. WOLFSON
JOSEPH FISCHER

BOOK REVIEWS

Medical Diagnosis: Applied physical diagnosis. Edited by Roscoe L. Pullen, M.D. With a foreword by John H. Musser, M.D. 8° cloth, 1106 pp., with 584 illustrations and 12 colored plates. Philadelphia and London: W. B. Saunders Company, 1944. \$10.00.

This book is intended to develop the ability of the physician to examine all parts of the body. Specialists have contributed chapters outlining the procedure appropriate for examinations within their special provinces.

This plan is excellent for an encyclopedia but has certain disadvantages when the material is compressed into a single volume intended for use as a textbook. One is tempted to ask why, if one man is expected to master the contents of the text, should not one man write it, thereby demonstrating the possibility of a single person's mastering the field covered by the book. Again, as a textbook, it is too advanced for the second-year student, who has not yet been introduced to much of the subject matter, whereas more detailed information is preferable for advanced or graduate students. Probably a physician or student is best equipped when he has mastered the fundamentals of simple physical diagnosis and then uses special manuals of electrocardiography, ophthalmology, gynecology, dermatology and so on for assistance in special fields.

Nevertheless, the work is as well done as one can reasonably demand, and its value is likely to be determined by the extent to which it is chosen by instructors and students.

Principles and Practices of Inhalational Therapy. By Alvan L. Barach, M.D. 8°, cloth, 315 pp., with 59 illustrations. Philadelphia: J. B. Lippincott Company, 1944. \$4.00.

This is an unusual book in that it represents in the main the studies of the author over a period of twenty-four years on the therapeutic use of gases in clinical medicine, comprising the results of over a hundred papers. It will be remembered that in 1925 Dr. Barach developed an oxygen tent ventilated by the passage of air over ice, which first provided a hygienic atmosphere in respect to temperature and humidity, as well as an effective concentration of oxygen. He introduced helium as a therapeutic gas in the treatment of asthma and obstructive dyspnea and, with the aid of skilled technical assistants, developed chambers, hoods and masks for the administration of oxygen and of helium and oxygen mixtures. His use of positive pressure in the treatment of obstructive dyspnea and pulmonary edema brought a new therapeutic procedure to clinical medicine. Of great interest is his method of immobilizing both lungs through equalizing the air pressure on the inner and outer surface of the chest wall; this equalizing pressure chamber has been employed on patients with advanced pulmonary tuberculosis with promising results.

A good description of the contributions of other workers in this field is included, together with an extensive bibliography.

The book describes in clear detail the use of oxygen, helium, carbon dioxide, positive pressure, continuous pulmonary arrest and vaporized solutions of epinephrine, Neo-Synephrin and sulfonamides as therapeutic agents for maintaining respiratory function. It is well illustrated with photographs of apparatus and with charts confirming the physiologic usefulness of various types of inhalational therapy.

Each chapter heading represents a disease entity, for example, pneumonia, pulmonary edema, bronchial asthma, shock, acute altitude sickness and so forth, and contains a discussion of the pathologic physiology, the specific inhalational therapy and the results to be expected. The chapters covering bronchial asthma, congestive heart failure, pulmonary emphysema and chronic pulmonary tuberculosis are beautifully written

and replete with the special disturbances in respiratory function involved and their management. Those interested in aviation medicine will find the chapter on acute altitude sickness, including many of the author's own observations, one of the best ever written on this timely subject.

This is the first complete textbook of its kind. The physician who wishes to understand the physiologic basis and technic of inhalational therapy will find it indispensable. To the student and research worker in the field it will serve as a bible, as well as a source of stimulation in the study of this fascinating, relatively new approach of therapy via the pulmonary route.

NOTICES

ANNOUNCEMENT

Dr. Oscar J. Marcil announces the removal of his office from East Jaffrey, New Hampshire, to 66 Parker Street, Gardner, Massachusetts.

BARUCH FELLOWSHIPS IN PHYSICAL MEDICINE

The Harvard Medical School announces fellowships in physical medicine supported by grants from the Baruch Committee on Physical Medicine. The purpose of these fellowships is to provide a three-year training for academic and clinical careers in the field of physical medicine. They are granted annually but subject to renewal for a total duration of three years. The first year will be wholly or in part devoted to basic research related to physical medicine in one of the preclinical sciences, such as physiology, anatomy or biophysics. The second year will be spent in clinical training in physical medicine at the Massachusetts General Hospital and other hospitals affiliated with the Harvard Medical School. In the third year fellows will be assistants in physical medicine with clinical responsibilities. For candidates with extensive previous training, one-year clinical fellowships will also be granted.

Applicants must have an M.D. degree from an approved medical school and a minimum of one year of internship in an approved hospital. The annual stipend will be \$2500 (single) or \$3000 (married). Applications may be obtained from the Dean, Harvard Medical School, 25 Shattuck Street, Boston 15, Massachusetts.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, January 3 — Surgical Difficulties in Ulcerative Colitis. Dr. Francis Moore.

Friday, January 5 — Cancer of the Cervix. Dr. B. Lorincz.
Wednesday, January 10 — The Incidence of Psychoneurosis in the Medical Clinic. Dr. Joseph Kaplan.

Friday, January 12 — Cancer of the Pancreas and Ampulla Relative to Diagnosis and Resection. Dr. Richard B. Cattell.

Wednesday, January 17 — Breast Cancer: Problems of diagnosis and treatment. Dr. Joseph Tartakoff.

Friday, January 19 — The History and Physical Examination of the Gynecological Patient. Dr. Louis E. Phaneuf.

Wednesday, January 24 — Studies of Finger Capillaries in Neuroses, Epilepsy, and Migraine. Dr. Alfred Hauptmann.

Friday, January 26 — The Treatment of Thyrotoxicosis with Anti-thyroid Drugs. Dr. R. Williams.

Wednesday, January 31 — A Recent Advance in Dermatological Therapy. Dr. Francis M. Thurmon.

On Monday mornings clinics will be given by Dr. Samuel Proger. On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings clinics will be given by Dr. William Dameshek.

(Notices continued on page 17)

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Number 26

THE CAUSE OF DEATH IN DIABETES*

A Report of 307 Autopsied Cases

STANLEY L. ROBBINS, M.D.,† AND ARTHUR W. TUCKER, JR., M.D.‡

BOSTON

A SEARCH through the literature for an answer to the question of the causes of death in diabetic patients reveals a large amount of available material, with surprisingly little of it based on pathological confirmation through autopsy examination. Analyses based on clinical findings alone and on diagnoses found on death certificates are filled with patent inaccuracies. Joslin¹ and others have repeatedly demonstrated that figures gathered from death certificates are subject to so many errors as to vitiate many of the conclusions drawn from them. The example of a cerebral hemorrhage found at autopsy as a cause of death in a case clinically diagnosed as a diabetic coma is a not infrequent occurrence. This report therefore represents an attempt to determine the causes of death in a series of diabetic patients from a strictly anatomic approach, comparable to the series of 486 diabetic autopsies reported by Warren.² It is believed that such statistical analyses based on anatomic findings give more accurate information regarding causes of death than do analyses based solely on clinical observations.

MATERIAL AND METHODS

The subject matter of this report is drawn from a study of 307 diabetic patients autopsied at the Mallory Institute of Pathology during the years 1932-1942, inclusive. Excluded from the study are a few cases in which the material was inadequate. In each case the complete protocol was reviewed and the available histologic material was examined to establish the anatomic cause of death. When more than one possibility presented itself, the clinical records were reviewed in an effort to understand more clearly the patient's terminal course. It is obvious that cases were met with in which no clear-cut conclusion could be drawn, either because of inadequate records or because of the fundamental

limitations of the anatomic approach. Such cases were discarded. The patients included 131 males and 176 females, ranging between the ages of thirteen and eighty-four.

As a basis for comparison, the anatomic causes of death in approximately 2800 autopsied nondiabetic patients were summarized. The control group represented all nondiabetic patients over twelve years of age coming to autopsy in the years 1936, 1937, 1941 and 1942, whole years being selected to avoid seasonal variations. These particular years were selected in an effort to represent both the pre-sulfonamide and post-sulfonamide eras, as well as changing therapies over the period of investigation.

Adequate histologic material was available in 268 of the diabetic cases. Routine sections of the liver, kidneys, pancreas and adrenal glands were studied in an effort to determine the frequency of specific histopathologic changes associated with the diabetes.

RESULTS

Table 1 indicates the distribution of the causes of death in the diabetic and control series. These various groups and subgroups were selected because they obviously represent the most frequent conditions of which diabetic patients — and for that matter nondiabetic ones — die. Certain of the headings used require a few words of explanation to clarify the type of case included within the category.

The term "peripheral vascular disease" is used to indicate the cases of vascular insufficiency leading to gangrene and death, either without infection or with infections so trivial as to constitute only a minor part of the clinical picture. In many of these cases, amputation was performed and was followed at some interval of time by death. If there was a clear-cut chain of circumstance pointing to the peripheral vascular disease as the initiating event in the fatal course, the death was listed in this category. On the other hand, infections of the extremities were separated from the above group because

*From the Mallory Institute of Pathology, Boston City Hospital.

†Teaching fellow in pathology, Mallory Institute of Pathology, instructor in pathology, Boston University School of Medicine.

‡Formerly, resident in pathology, Mallory Institute of Pathology.

Surely there must be something wrong when the *New England Journal of Medicine* reviews a book more than a year after all the other medical journals mentioned above, all of them having received the book at the same time. The complete lack of agreement of the *Journal's* review with those of the other periodicals can of course not be commented upon, but it raises questions as to the correctness of the reviewer's opinions as expressed in the *New England Journal of Medicine*.

LOUIS E. WOLFSON
JOSEPH FISCHER

BOOK REVIEWS

Medical Diagnosis: Applied physical diagnosis. Edited by Roscoe L. Pullen, M.D. With a foreword by John H. Musser, M.D. 8°, cloth, 1106 pp., with 584 illustrations and 12 colored plates. Philadelphia and London: W. B. Saunders Company, 1944. \$10.00.

This book is intended to develop the ability of the physician to examine all parts of the body. Specialists have contributed chapters outlining the procedure appropriate for examinations within their special provinces.

This plan is excellent for an encyclopedia but has certain disadvantages when the material is compressed into a single volume intended for use as a textbook. One is tempted to ask why, if one man is expected to master the contents of the text, should not one man write it, thereby demonstrating the possibility of a single person's mastering the field covered by the book. Again, as a textbook, it is too advanced for the second-year student, who has not yet been introduced to much of the subject matter, whereas more detailed information is preferable for advanced or graduate students. Probably a physician or student is best equipped when he has mastered the fundamentals of simple physical diagnosis and then uses special manuals of electrocardiography, ophthalmology, gynecology, dermatology and so on for assistance in special fields.

Nevertheless, the work is as well done as one can reasonably demand, and its value is likely to be determined by the extent to which it is chosen by instructors and students.

Principles and Practices of Inhalational Therapy. By Alvan L. Barach, M.D. 8°, cloth, 315 pp., with 59 illustrations. Philadelphia: J. B. Lippincott Company, 1944. \$4.00.

This is an unusual book in that it represents in the main the studies of the author over a period of twenty-four years on the therapeutic use of gases in clinical medicine, comprising the results of over a hundred papers. It will be remembered that in 1925 Dr. Barach developed an oxygen tent ventilated by the passage of air over ice, which first provided a hygienic atmosphere in respect to temperature and humidity, as well as an effective concentration of oxygen. He introduced helium as a therapeutic gas in the treatment of asthma and obstructive dyspnea and, with the aid of skilled technical assistants, developed chambers, hoods and masks for the administration of oxygen and of helium and oxygen mixtures. His use of positive pressure in the treatment of obstructive dyspnea and pulmonary edema brought a new therapeutic procedure to clinical medicine. Of great interest is his method of immobilizing both lungs through equalizing the air pressure on the inner and outer surface of the chest wall; this equalizing pressure chamber has been employed on patients with advanced pulmonary tuberculosis with promising results.

A good description of the contributions of other workers in this field is included, together with an extensive bibliography.

The book describes in clear detail the use of oxygen, helium, carbon dioxide, positive pressure, continuous pulmonary arrest and vaporized solutions of epinephrine, Neo-Synephrin and sulfonamides as therapeutic agents for maintaining respiratory function. It is well illustrated with photographs of apparatus and with charts confirming the physiologic usefulness of various types of inhalational therapy.

Each chapter heading represents a disease entity, for example, pneumonia, pulmonary edema, bronchial asthma, shock, acute altitude sickness and so forth, and contains a discussion of the pathologic physiology, the specific inhalational therapy and the results to be expected. The chapters covering bronchial asthma, congestive heart failure, pulmonary emphysema and chronic pulmonary tuberculosis are beautifully written

and replete with the special disturbances in respiratory function involved and their management. Those interested in aviation medicine will find the chapter on acute altitude sickness, including many of the author's own observations, one of the best ever written on this timely subject.

This is the first complete textbook of its kind. The physician who wishes to understand the physiologic basis and technic of inhalational therapy will find it indispensable. To the student and research worker in the field it will serve as a bible, as well as a source of stimulation in the study of this fascinating, relatively new approach of therapy via the pulmonary route.

NOTICES

ANNOUNCEMENT

Dr. Oscar J. Marcil announces the removal of his office from East Jaffrey, New Hampshire, to 66 Parker Street, Gardner, Massachusetts.

BARUCH FELLOWSHIPS IN PHYSICAL MEDICINE

The Harvard Medical School announces fellowships in physical medicine supported by grants from the Baruch Committee on Physical Medicine. The purpose of these fellowships is to provide a three-year training for academic and clinical careers in the field of physical medicine. They are granted annually but subject to renewal for a total duration of three years. The first year will be wholly or in part devoted to basic research related to physical medicine in one of the preclinical sciences, such as physiology, anatomy or biophysics. The second year will be spent in clinical training in physical medicine at the Massachusetts General Hospital and other hospitals affiliated with the Harvard Medical School. In the third year fellows will be assistants in physical medicine with clinical responsibilities. For candidates with extensive previous training, one-year clinical fellowships will also be granted.

Applicants must have an M.D. degree from an approved medical school and a minimum of one year of internship in an approved hospital. The annual stipend will be \$2500 (single) or \$3000 (married). Applications may be obtained from the Dean, Harvard Medical School, 25 Shattuck Street, Boston 15, Massachusetts.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, January 3 — Surgical Difficulties in Ulcerative Colitis. Dr. Francis Moore.

Friday, January 5 — Cancer of the Cervix. Dr. B. Lorincz.
Wednesday, January 10 — The Incidence of Psychoneurosis in the Medical Clinic. Dr. Joseph Kaplan.

Friday, January 12 — Cancer of the Pancreas and Ampulla Relative to Diagnosis and Resection. Dr. Richard B. Cattell.

Wednesday, January 17 — Breast Cancer: Problems of diagnosis and treatment. Dr. Joseph Tartakoff.

Friday, January 19 — The History and Physical Examination of the Gynecological Patient. Dr. Louis E. Phaneuf.

Wednesday, January 24 — Studies of Finger Capillaries in Neuroses, Epilepsy, and Migraine. Dr. Alfred Hauptmann.

Friday, January 26 — The Treatment of Thyrotoxicosis with Anti-thyroid Drugs. Dr. R. Williams.

Wednesday, January 31 — A Recent Advance in Dermatological Therapy. Dr. Francis M. Thurmon.

On Monday mornings clinics will be given by Dr. Samuel Proger. On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings clinics will be given by Dr. William Dameshek.

(Notices continued on page 865)

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THE CAUSE OF DEATH IN DIABETES*

A Report of 307 Autopsied Cases

STANLEY L. ROBBINS, M.D.,† AND ARTHUR W. TUCKER, JR., M.D.‡

BOSTON

SEARCH through the literature for an answer to the question of the causes of death in diabetic patients reveals a large amount of available material, with surprisingly little of it based on histological confirmation through autopsy examination. Analyses based on clinical findings alone and diagnoses found on death certificates are filled with patent inaccuracies. Joslin¹ and others have repeatedly demonstrated that figures gathered from death certificates are subject to so many errors as to vitiate many of the conclusions drawn from them. The example of a cerebral hemorrhage found at autopsy as a cause of death in a case clinically diagnosed as a diabetic coma is a not infrequent occurrence. This report therefore represents an attempt to determine the causes of death in a series of diabetic patients from a strictly anatomic approach, comparable to the series of 486 diabetic autopsies reported by Warren.² It is believed that such statistical analyses based on anatomic findings will give more accurate information regarding causes of death than do analyses based solely on clinical observations.

MATERIAL AND METHODS

The subject matter of this report is drawn from a study of 307 diabetic patients autopsied at the Mallory Institute of Pathology during the years 1932-1942, inclusive. Excluded from the study are a few cases in which the material was inadequate. In each case the complete protocol was reviewed and the available histologic material was examined to establish the anatomic cause of death. When more than one possibility presented itself, the clinical records were reviewed in an effort to understand more clearly the patient's terminal course. It is obvious that cases were met with in which no clear-cut conclusion could be drawn, either because of inadequate records or because of the fundamental

limitations of the anatomic approach. Such cases were discarded. The patients included 131 males and 176 females, ranging between the ages of thirteen and eighty-four.

As a basis for comparison, the anatomic causes of death in approximately 2800 autopsied nondiabetic patients were summarized. The control group represented all nondiabetic patients over twelve years of age coming to autopsy in the years 1936, 1937, 1941 and 1942, whole years being selected to avoid seasonal variations. These particular years were selected in an effort to represent both the pre-sulfonamide and post-sulfonamide eras, as well as changing therapies over the period of investigation.

Adequate histologic material was available in 268 of the diabetic cases. Routine sections of the liver, kidneys, pancreas and adrenal glands were studied in an effort to determine the frequency of specific histopathologic changes associated with the diabetes.

RESULTS

Table 1 indicates the distribution of the causes of death in the diabetic and control series. These various groups and subgroups were selected because they obviously represent the most frequent conditions of which diabetic patients—and for that matter nondiabetic ones—die. Certain of the headings used require a few words of explanation to clarify the type of case included within the category.

The term "peripheral vascular disease" is used to indicate the cases of vascular insufficiency leading to gangrene and death, either without infection or with infections so trivial as to constitute only a minor part of the clinical picture. In many of these cases, amputation was performed and was followed at some interval of time by death. If there was a clear-cut chain of circumstance pointing to the peripheral vascular disease as the initiating event in the fatal course, the death was listed in this category. On the other hand, infections of the extremities were separated from the above group because

From the Mallory Institute of Pathology, Boston City Hospital.
Teaching fellow in pathology, Mallory Institute of Pathology, instructor in pathology, Boston University School of Medicine.
Formerly, Mallory Institute of Pathology.

it was thought that, despite the underlying vascular insufficiency that some of these patients had, the clinical picture was dominated by the superimposed infection. The patients showed essentially febrile

TABLE 1.

CAUSE OF DEATH	DIABETIC GROUP		NONTIA-BETIC GROUP	
	NO OF CASES	PER-CENTAGE	RECTED PER-CENTAGE*	PER-CENTAGE
Coma	22	7.2	—	—
Vascular disease:				
Cardiac decompensation	35	11.4	12.3	12.6
Coronary occlusion	31	10.0	10.8†	4.2†
Cerebral hemorrhage and thrombosis	15	4.9	5.2	7.5
Peripheral vascular disease	13	4.2	4.5†	0.0†
Central (pulmonary embolism)	7	2.3	2.4	2.8
Renal disease:				
Glomerulonephritis	2	0.7	0.7	0.4
Acute pyelonephritis	21	6.8	7.3†	1.6†
Miscellaneous	2	0.7	0.7	2.0
Infection:				
Pulmonary	73	23.8	25.6	24.2
Peritoneal	13	4.2	4.5	4.8
Extremities	7	2.3	2.4†	0.5†
Other infections	22	7.2	7.7	5.9
Cancer	24	7.8	8.4†	14.7†
Other causes (including unknown)	20	6.5	7.0	17.0

*From a statistical viewpoint, in order to compare the diabetic and control groups, it is necessary to eliminate coma cases from the comparison, since they are a hazard peculiar only to the diabetic patient and are not found in a series of control cases. This column, therefore, represents the diabetic series from which coma cases have been excluded, the mortality percentage being recomputed in order that they may be strictly comparable with those of the control group.

†Denotes statistically significant differences.

reactions, often with spreading sepsis, septicemia and death.

The term "pulmonary infection" indicates a wide variety of inflammatory diseases of the lung, such as bronchiectasis, lung abscess, pneumonia and tuberculosis, no attempt being made to separate this heterogeneous collection into its component parts.

In the interests of simplicity, unknown causes of death, traumatic deaths, anemias and a diversity of the less frequent fatal diseases have been grouped under the heading "other causes."

The most frequent cause of death in the diabetic group was pulmonary infection (25.6 per cent); cardiac decompensation and coronary occlusion follow with 12.3 per cent and 10.8 per cent, respectively. The relative frequency of fatal carcinoma is seen to be 8.4 per cent. That of acute pyelonephritis, decompensated, was 7.3 per cent, and that of uncomplicated coma 7.2 per cent. Cerebral vascular disease was found to be relatively low in the scale, accounting for only 5.2 per cent of the deaths.

In the control group pulmonary infection again led with 24.2 per cent. Deaths due to carcinoma were second with 14.7 per cent. Cardiac decompensation followed with 12.6 per cent, whereas coronary occlusion and acute pyelonephritis were significantly far down on the list, with 4.2 and 1.6 per cent, respectively.

Table 2 indicates the frequency of certain histopathologic changes in the diabetic group. These lesions were arbitrarily designated as + to + + + +, only changes of ++ or greater being considered

significant. Evidence of cirrhosis was found in 27 of the 268 cases; the type was alcoholic cirrhosis in 13, biliary cirrhosis in 11, and healed acute yellow atrophy in 3.

Finally, as has been shown before,^{3, 4} the average age at death of the diabetic patients in this series was not significantly different from that of the non-diabetic, being 59.6 years in the former and 59.8 years in the latter.

DISCUSSION

In considering the figures presented, one must bear in mind that they are derived from a large municipal hospital, accepting all varieties of cases, many already in terminal or near-terminal stages, together with emergency cases combed from a wide metropolitan area. For example, the apparent high incidence of pulmonary infection as a cause of death as compared with that in other series is due in part to the fact that the hospital annually receives a significant number of cases of pulmonary tuberculosis. In the diabetic group, 17 of the 73 fatal pulmonary infections were tuberculous, representing a frequency of 5.6 per cent or 6.0 per cent when corrected for coma. A comparison with the 8 per cent incidence found in the control group reveals no significant difference between the two groups. Similarly, deaths from coma (7.2 per cent) occupy

TABLE 2. Selected Histologic Findings in 268 Diabetic Patients

LESION	DEGREE OF CHANGE					SIGNIFICANT CHANGE %
	++++	+++	++	+	NONE	
Kidneys:						
Glycogen nephrosis	17	44	43	14	39	42
Benign nephrosclerosis	29	50	58	19	93	55
Inter-capillary glomerulo-sclerosis	7	23	21	3	201	20
Pancreas:						
Hyalinization or fibrosis of islets	8	24	34	12	106	36
Liver:						
Nuclear glycogen	27	54	60	20	53	56
Fat	13	22	34	30	41	48

a higher rank in the causes of death in the present series than that found in other published series because some of the patients were not infrequently first seen in far-advanced coma at a stage in which the process had perhaps become irreversible.

On the other hand, the relatively low incidence of coronary occlusion as a cause of death (10.8 per cent) may be in part attributable to two factors. In the first place, in this laboratory the assignment of coronary occlusion as a cause of death is not made unless the myocardial infarction is significantly large, or unless there is a clear-cut terminal clinical course that corroborates the finding of an occluded coronary artery in cases in which the process has been too recent for the development of a massive infarction. In the second place, a certain percentage of acute coronary deaths are handled by the Medical Examiner's Office and hence are not available for inclusion within this series.

Perhaps worthy of emphasis is the finding of a relatively similar incidence of cerebrovascular accidents as a cause of death in the diabetic and nondiabetic groups — 5.2 per cent and 7.5 per cent, respectively. This finding is in agreement with that of Root and Sharkey,⁵ who state that the non-vascular cerebral arteries have no greater predisposition to atherosclerosis in diabetic than in nondiabetic patients.

A point of further interest is that there was a lower incidence of death from carcinoma in the diabetic group (8.4 per cent) than in the control group (14.7 per cent). In view of the close similarity of the survival age in the two groups, age does not seem to aid in accounting for the difference, and at present no other factor appears to be implicated. It is particularly noteworthy in view of the present interest in the relation of cholesterol and of hypercholesterolemic states to the production of neoplasia. A comparison of the figures reveals other significant differences in only four categories, namely, coronary occlusion, peripheral vascular disease, acute pyelonephritis and infections of the extremities.

Considering each of these separately, one finds that coronary occlusion was two and a half times as frequent in the diabetic group as in the control group. Peripheral vascular disease, although a rarity among nondiabetic patients, accounted for 1.5 per cent of the deaths among diabetic patients, which confirms a well-known fact previously emphasized. A similar situation obtains with reference to infections of the extremities, in which the admonitions of Joslin⁶ are borne out by the greater frequency with which this complication leads to death among diabetic patients than among nondiabetic ones. Finally, renal infection, which for many years has been considered a minor complication, is seen to be a relatively important cause of death in the diabetic group. Acute pyelonephritis was four and a half times as frequent a cause of death in the diabetic group as in the control group, and moreover ranks sixth among the causes of death in the former group.

The six most frequent causes of death in the two groups are listed in Table 3.

In Warren's series of 486 autopsies on diabetic patients who died during the years 1924–1937, in-

cerebral arteriosclerosis accounted for 4 per cent of the deaths. The percentage of patients dying of pulmonary infections was 10 per cent, with pyelonephritis occupying a low place on the list of total causes, accounting for only 2 deaths.

In an evaluation of the histologic material presented in Table 2, it can be seen that each of the findings is relatively inconstant. Not only were most of the histologic changes haphazard in their occurrence, but all save one were nonspecific from a diagnostic standpoint.

At this laboratory, only glycogen nephrosis or so-called "Armanni-Ebstein cells" in the tubular epithelium of the loops of Henle are considered diagnostic of diabetes mellitus. It is noteworthy that this change was evident to a significant degree in only 42 per cent of the cases. It may be of some interest to note that with the passing years the finding of glycogen nephrosis has become increasingly less frequent, suggesting that adequate therapy may prevent this type of secondary lesion. Inter-capillary glomerulosclerosis was present in only 20 per cent of the cases.

Although nuclear changes of the liver cells were the most frequent histologic feature, occurring in 66 per cent of the series, the complete nonspecificity of such changes lends them little significance.

During the eleven years covered by this survey, 45 cases of pigment cirrhosis were autopsied. These cases are not included in the diabetic group inasmuch as the diabetes associated with this disease is considered by all the standard classifications of disease as an entity distinct from diabetes mellitus. Included in the 268 cases studied microscopically, however, were 27 cases with incidental cirrhosis, apparently only coincidental with and in no way specifically related to the diabetes.

It should be re-emphasized that the average age at death of the diabetic patient is almost precisely the same as that of the nondiabetic one. He lives as long today as the latter, but, as brought out by this survey, there are specific hazards that the diabetic patient is more likely to encounter than the nondiabetic, namely, coronary occlusion, peripheral vascular disease, infections of the extremities and acute pyelonephritis.

SUMMARY AND CONCLUSIONS

An analysis of the causes of death in 307 diabetic patients over the age of twelve, as determined by autopsy findings, is presented.

For purposes of comparison, the autopsies on approximately 2800 consecutive nondiabetic patients were reviewed for anatomic causes of death.

Adequate histologic material available in 268 of the patients in the diabetic group was reviewed to evaluate the frequency of histopathologic changes in diabetes.

From the study, several clinical impressions were confirmed. The diabetic patient lives as long as the

TABLE 3. Most Frequent Causes of Death in Diabetic and Nondiabetic Patients.

DIABETIC PATIENTS		NONDIABETIC PATIENTS	
CAUSE OF DEATH	PERCENTAGE	CAUSE OF DEATH	PERCENTAGE
Pulmonary infection	25.6	Pulmonary infection	24.2
Cardiac decompensation	12.3	Carcinoma	14.7
Coronary occlusion	10.8	Cardiac decompensation	12.6
Carcinoma	8.4	Cerebral accident	7.5
Infections, not pulmonary, peritoneal or of extremities	7.7	Infections, not pulmonary, peritoneal or of extremities	5.9
Acute pyelonephritis	7.5	Peritoneal infection	4.8

clusive, coma was present in 127 cases, or 26 per cent. Arteriosclerotic cardiac lesions were the cause of death in 17 per cent of the patients, whereas

it was thought that, despite the underlying vascular insufficiency that some of these patients had, the clinical picture was dominated by the superimposed infection. The patients showed essentially febrile

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significant. Evidence of cirrhosis was found in 2 of the 268 cases; the type was alcoholic cirrhosis in 13, biliary cirrhosis in 11, and healed acute yellow atrophy in 3.

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CLINICAL COURSE

By far the most frequent history was one of sudden onset one day before admission; this was present in 42 cases (59 per cent). In 18 cases the onset occurred two days before admission, in 10 cases three days before admission, and in 2 cases more than four days.

The chief complaint on admission was persistent and often projectile vomiting in 46 cases (64 per cent), headache — either as a principal or a secondary complaint — in 23, stiff neck in 12, a rash in

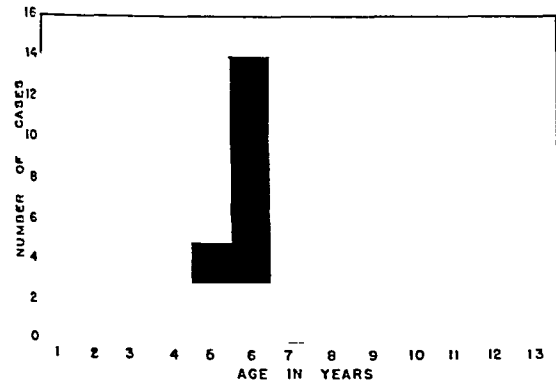


FIGURE 2. Age Distribution.

10, and drowsiness in 10. The other chief complaints were as follows: convulsions (8 cases), fever (7 cases), delirium (7 cases), abdominal pain (4 cases), arthralgia (3 cases), myalgia (2 cases) and coma (2 cases).

In 59 cases (82 per cent) a rash was observed on admission. This appeared to be one of the most distinctive features of the disease. The skin eruption was purpuric in nature, resembling the so-called "flea-bite." These petechial hemorrhages occurred very early in the course of the disease, and in many cases multiplied rapidly within a short space of time. They usually appeared on the arms and legs, especially about the ankles. In one case the lesions were maculopapular, resembling the rash present in measles. The diameter of the hemorrhages varied from pinhead size to 3 or 4 cm., the larger ones having necrotic centers. A characteristic of this eruption was the occurrence of the petechial hemorrhages in the mucous membranes of the mouth and eyes, and also on the skin of the palms and soles. This fact was helpful in diagnosing the disease in Negroes, whose skin is lighter on the palms and soles than on the rest of the body, making the eruptions easy to detect.

The cause of this petechial rash is believed to be small, septic, vascular thrombi that form in the small capillaries, causing extravasation of blood into the surrounding tissue.^{13, 14} The organisms can be cultured from these spots and can also be directly visualized by the technic outlined by Tompkins.¹⁵

There has been some speculation why the meningococcus has a predilection for the skin and — in the case of the Waterhouse-Friderichsen syndrome — the adrenal glands. Sacks¹⁶ thinks that the meningococcus has an ectodermal tropism that accounts for this. In most cases the hemorrhages faded appreciably within twenty-four hours after treatment and in three days little residual discoloration remained on the skin.

Convulsions were limited almost entirely to patients under three years of age. They occurred in 10 of the 14 one-year-old children, in 4 of the 12 two-year-olds, and in 2 of the 7 three-year-olds. Of the patients over the age of three, only one had a convulsion — a girl of twelve who was treated empirically at home for three days, was admitted in a moribund state and died shortly thereafter.

All the children over one year of age with evidence of meningeal infection had positive meningeal signs, but in most infants no such signs could be elicited. The patients most difficult to evaluate were those less than one year old, apparently because a slight spasm of the muscles is often difficult to detect. A more reliable index is the tension of the anterior fontanelle, which directly reflects the intracranial pressure.

Ten children were drowsy on admission, but only 2 were comatose. Hyperesthesia was present in almost all cases, and in many of them was so severe that the patient objected to any movement of the bed sheets or change in position. Myalgia and arthralgia were frequent complaints on admission. One patient had had such prominent joint symptoms that he was referred to the hospital with a diagnosis of rheumatic fever. Fifty-six patients (77 per cent) were admitted with a temperature of over 102°F.

The Waterhouse-Friderichsen syndrome is characterized by the fulminating onset of a petechial or purpuric skin eruption, a peculiar dyspnea and cyanosis and profound peripheral circulatory collapse.¹⁴ Death usually ensues after a short period of illness. Bilateral adrenal hemorrhage is found at autopsy, and is believed to be the cause of this condition. Nine patients (12 per cent) presented this symptomatology. Of these, 4, one of whom had a meningococcemia, eventually recovered after intensive treatment. Of the 5 patients who died, 2 had meningococcemia. Evidence of adrenal hemorrhage was found in the 3 fatal cases that were autopsied.

In the total series there were 6 deaths, a mortality of 8 per cent. This figure should be qualified, since 5 of these patients were admitted in a moribund state and lived only thirteen hours or less under treatment. As previously mentioned, 5 of the fatal cases showed symptoms similar to those described as the Waterhouse-Friderichsen syndrome. The other patient, although in coma, was neglected at home

nondiabetic. There are, however, certain hazards that he is seemingly more likely to encounter, namely, coronary occlusion, peripheral vascular disease, infections of the extremities and acute pyelonephritis.

We are indebted to Professor G. Wadsworth, of the Massachusetts Institute of Technology, for statistical analyses of the figures.

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MENINGOCOCCAL MENINGITIS AND MENINGOCOCCEMIA IN CHILDHOOD*

A Statistical Study of Seventy-Two Cases

JOSEPH OSBORNE, M.D.,† WILLIAM H. ARNONE, M.D.,‡ AND GEORGE I. LYTHCOTT, II, M.D.§

BOSTON

MENINGOCOCCAL meningitis, also known as spotted fever or cerebrospinal fever, first accurately described in 1805 by Vieusseux,¹ is always more prevalent during time of war than in peacetime. During World War I, 5839 cases occurring in the armed forces resulted in 2279 deaths, a mortality of 39 per cent.² Judging from reports in the recent literature, two facts are apparent: first, that the high incidence of this disease is being repeated, and second, that the use of the sulfonamide drugs has greatly reduced the mortality.^{3, 4} Concurrent with the increase of meningococcal meningitis among the military population is an increase among civilians, including children.⁵

During 1943, on the Pediatric Service of the Boston City Hospital, there was a marked increase in the number of children, all under twelve years of age, having meningococcal meningitis or meningococcemia. It seemed that a review of these cases would bring attention to the prevalence of this disease among the younger population and would be valuable to those engaged in the treatment of children with this type of infection.

ETIOLOGY

The etiologic agent of this disease is the meningococcus, which was discovered by Weichselbaum in 1887.⁶ There are several strains of meningococci that can be demonstrated by immunologic reactions. Gordon and Murray⁷ originally described four serologic types, but it is now generally conceded that the majority of pathogenic strains fall into Types 1, 2 and 2a. The typing is achieved by mixing the meningococcus with type-specific serum⁸ and noting the resulting capsular swelling or agglutination.

The question how the organism enters the body is still a matter of dispute. Some observers have postulated that the meningococcus invades the central nervous system by way of the cribriform plate.⁹ The most widely accepted theory, however, is that the bacteria penetrate the mucous membranes of the nose and nasopharynx before entering the blood stream.^{10, 11}

INCIDENCE

As shown in Figure 1, the seasonal peak was reached during the spring and late fall, with a drop

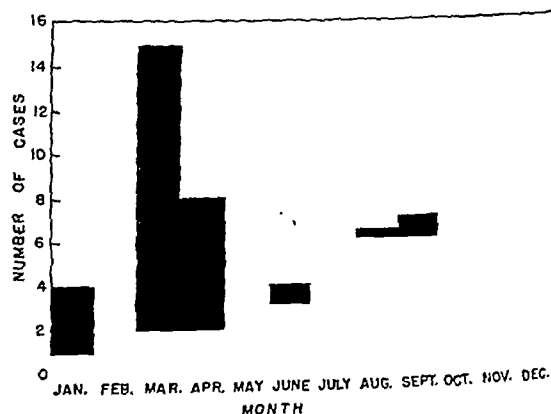


FIGURE 1. Monthly Incidence.

during the summer. This coincides with the seasonal incidence of upper respiratory infections.

The disease was somewhat more prevalent among girls than among boys, the respective numbers of cases being 40 and 32.

Fourteen cases (19 per cent) occurred in those under one year of age, the youngest patient being nineteen days old, and 41 (56 per cent) in those under five years of age (Fig. 2). This coincides with the report of Holt and McIntosh,¹² who noted a high incidence of the disease in those under five years old.

*From the Pediatric Service of the Boston City Hospital, and the Department of Pediatrics, Boston University School of Medicine.

†Formerly, resident physician, Boston City Hospital.

‡Resident physician, Boston City Hospital.

§Assistant resident physician, Boston City Hospital.

tients were afebrile one week after treatment, and 36 reached a normal temperature and a general feeling of improvement in four days (Fig. 3).

COMPLICATIONS

Arthritis was the most frequent complication encountered, 9 cases (12 per cent) showing evidence of it. This is a somewhat higher incidence than was

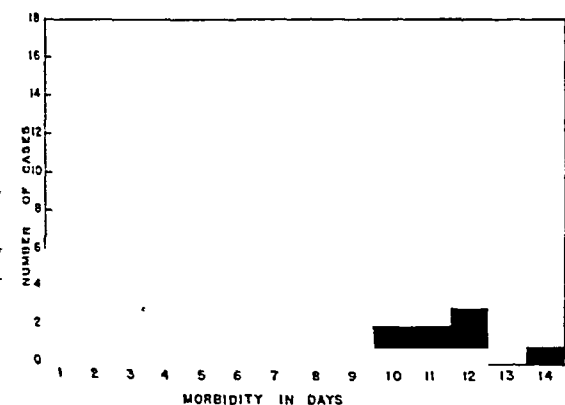


FIGURE 3. Morbidity.

reported in Boulduan's series cited by Schein,²⁰ in which 13 of 169 patients (7.7 per cent) manifested arthritic signs. The elbow was affected in 7 cases, the knees in 4, and the wrists in 2. Polyarthritis was noted in 4 cases. The average time for the joint manifestations to appear was six days after the onset of the disease. The duration of actual symptoms was eight and a half days. The only treatment required to gain complete function and recovery was immobilization of the involved joint with splints and a flannel bandage. Passive motion and physiotherapy were instituted as soon as it was thought that active inflammation of the joint had subsided. The arthritis appeared to be periartritic, with thickening and inflammation about the joint but no active suppuration within the joint itself. This is in agreement with the observations of Herrick and Parkhurst.²¹

One case of purulent conjunctivitis, having Type 1 meningococci as the etiologic agent, was observed in a boy of eleven. Boric irrigations and sulfadiazine orally cleared the conjunctivitis, as well as the meningitis, without any complications.

A boy of nine developed complete aphasia one week after hospitalization. This gradually cleared without treatment, leaving no residual signs.

SUMMARY

A series of 72 cases of meningococcal infection in children is presented.

Most cases gave a story of acute onset, ushered in by nausea and vomiting, headache, stiff neck and a skin rash. This rash was a valuable aid in the diagnosis of meningococcemia.

Neurologic symptoms were present in all cases having meningeal involvement. Whereas children under three often had convulsions, older children rarely did.

The predominant type of organism was a Type 1 meningococcus, occurring in 76 per cent of the cases in which cultures were positive.

All cases were treated with sulfadiazine.

The most frequent complication was arthritis, occurring in 12 per cent of the cases. Complete recovery from the arthritis resulted in all cases.

A mortality of 8 per cent occurred, all but 1 of the 6 fatal cases being of the Waterhouse-Friderichsen type. Four children with this syndrome survived.

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for three days before hospitalization and died shortly after admission.

LABORATORY FINDINGS

A lumbar puncture was performed on every patient. Ten cases (7 per cent) showed no organisms in the spinal fluid and were therefore classified as meningococcemia without meningitis; six of these patients were under four years of age. Sixty-two patients had a cloudy spinal fluid, with an average count of 6620 cells, 40 to 98 per cent of which were polymorphonuclear (leukocytes).

The sugar content was measured by the rapid method described by Alexander,¹⁷ which has proved extremely reliable and timesaving, being especially valuable at night when ordinary laboratory facilities are unavailable. Absence or diminution of sugar was found in all purulent spinal fluids.

Despite the presence of pus, in 13 cases (29 per cent), the fluid was sterile on culture. Of these cases, 5 exhibited intracellular and extracellular gram-negative diplococci on smear. In the 59 cases in which meningococci were recovered from the spinal fluid or blood, they proved to be Type 1 in 55 (76 per cent) and Type 2a in 4 (5 per cent).

The white-cell count on admission averaged 18,050, with a range of 8200 to 39,100. The blood cultures of 24 patients (33 per cent) failed to grow meningococci, although these organisms were isolated from the spinal-fluid culture or visualized on direct smear from the petechiae in most of these cases. The fact that bacteremia exists in the early stage of the disease and is transitory possibly accounts for the many negative blood cultures.¹⁸ No significant anemia directly attributable to the disease could be demonstrated.

TREATMENT

Prompt and adequate treatment in this disease is imperative and often lifesaving. The entire series of cases was treated with sulfadiazine, orally, subcutaneously or intravenously. In many cases all three methods were employed.

The following outline is a summary of the treatment used in all cases:

A lumbar puncture was done on all suspected cases. If purulent fluid was found, 10 to 20 cc. was removed to reduce the intracranial pressure. This procedure often transformed a disoriented, irritable child into a quiet, sleeping one. The spinal fluid was drained into three sterile tubes, — one for culture, one for a cell count and one for the determination of sugar, chloride and globulin.

Blood for culture and for a white-cell count was taken.

Sodium sulfadiazine was then given by slow intravenous drip in a dosage of 33 to 44 mg. ($\frac{1}{2}$ to $\frac{3}{4}$ gr.) per pound of body weight. In the

case of small children, where there is often technical difficulty in administering intravenous therapy, it was found that subcutaneous sodium sulfadiazine was useful. This drug when given in normal saline solution, diluted not to exceed 5 per cent concentration, produces blood levels of 10 to 12 mg. per 100 cc. in half an hour (Jorgensen and Greeley¹⁹).

Intravenous 5 per cent glucose in normal saline solution was then given to combat the almost universal acidosis and ketosis.

When the blood pressure was low and evidence of the Waterhouse-Friderichsen syndrome was present, 5 cc. of adrenocortical extract was given. This was put into a solution of 15 per cent glucose in normal saline solution and administered by slow intravenous infusion every four hours. The salt and glucose were given to restore the electrolyte imbalance and the depletion of glycogen stores. Synthetic desoxycorticosterone was also given in oily solution intramuscularly.

Sedation was used if the patient continued to be restless. The barbiturates, given either rectally or parenterally, proved to be satisfactory. Lumbar puncture and consequent relief of intracranial pressure, however, seemed to relax the patients enough so that little sedation was needed.

Six hours after the parenteral sulfadiazine had been given, oral sulfadiazine was administered and in most cases was retained without vomiting. This treatment was continued with 10 mg. (1/6 gr.) per pound of body weight every four hours.

If a patient showed evidence of recurrent intracranial pressure by convulsions, persistent vomiting, restlessness or irritability, a lumbar puncture was performed as often as once every four or six hours.

The following day a routine lumbar puncture was done and the spinal fluid was examined for cells, sugar and organisms. It was found that the sugar is the most reliable index of therapy, for if the spinal fluid has been sterilized, the sugar is almost always at a normal or near-normal level.

The urine was closely watched for evidence of sulfadiazine crystals or hematuria. Should these appear, fluids were forced immediately by mouth as well as intravenously, to promote diuresis. Sodium bicarbonate by mouth was also useful in promoting a more alkaline urine. If the urinary findings persisted, however, a shift to the more soluble sulfanilamide was made.

The average duration of chemotherapy was ten days. Sulfadiazine blood levels were determined on alternate days while the drug was being administered. A level of 10 to 12 mg. per 100 cc. was considered adequate.

Following the above treatment, a striking fall in temperature was usually noted. Forty-five pa-

patients were afebrile one week after treatment, and 36 reached a normal temperature and a general feeling of improvement in four days (Fig. 3).

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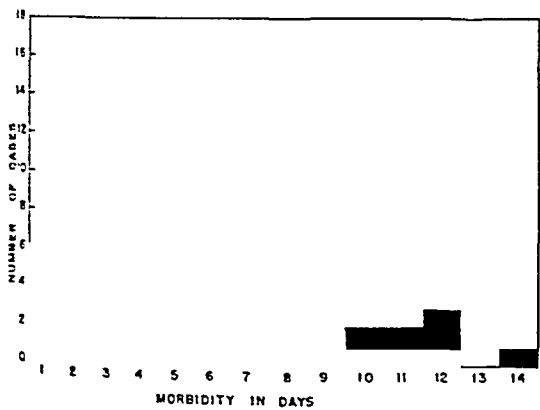


FIGURE 3. Mortality.

reported in Boulduan's series cited by Schein.²⁰ In which 13 of 169 patients (7.7 per cent) manifested joint signs. The elbow was affected in 7 cases, knees in 4, and the wrists in 2. Polyarthritis was noted in 4 cases. The average time for the joint manifestations to appear was six days after the onset of the disease. The duration of actual symptoms was eight and a half days. The only treatment required to gain complete function and recovery was immobilization of the involved joint with casts and a flannel bandage. Passive motion and physiotherapy were instituted as soon as it was thought that active inflammation of the joint had subsided. The arthritis appeared to be periartritic, with thickening and inflammation about the joint but no active suppuration within the joint itself. This is in agreement with the observations of Merrick and Parkhurst.²¹ One case of purulent conjunctivitis, having Type I meningococci as the etiologic agent, was observed in a boy of eleven. Boric irrigations and sulfadiazine orally cleared the conjunctivitis, as well as the meningitis, without any complications. A boy of nine developed complete aphasia one week after hospitalization. This gradually cleared without treatment, leaving no residual signs.

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SURGICAL MEASURES IN DYSMENORRHEA*

LOUIS E. PHANEUF, M.D., Sc.D.†

BOSTON

DYSMENORRHEA, or painful menstruation, is a symptom and not a primary disease. It is referred to as primary when no gross anatomic lesions can be found to account for it, and as secondary when organic disease of the pelvic organs or organs adjacent to them is responsible for the pain. In either case, when the symptom is mild to moderate, relief may be obtained by means of rest, the application of heat to the lower abdomen and the

metrium that is responsible for the improvement. The use of the intrauterine stem or pessary, which carried considerable vogue a quarter of a century ago, has fortunately been almost entirely abandoned. This instrument, which was sutured to the cervix and left in the uterus for a period of one to three months, did relieve the pain of menstruation in a number of cases, but, as might be expected, it was not infrequently followed by serious pelvic

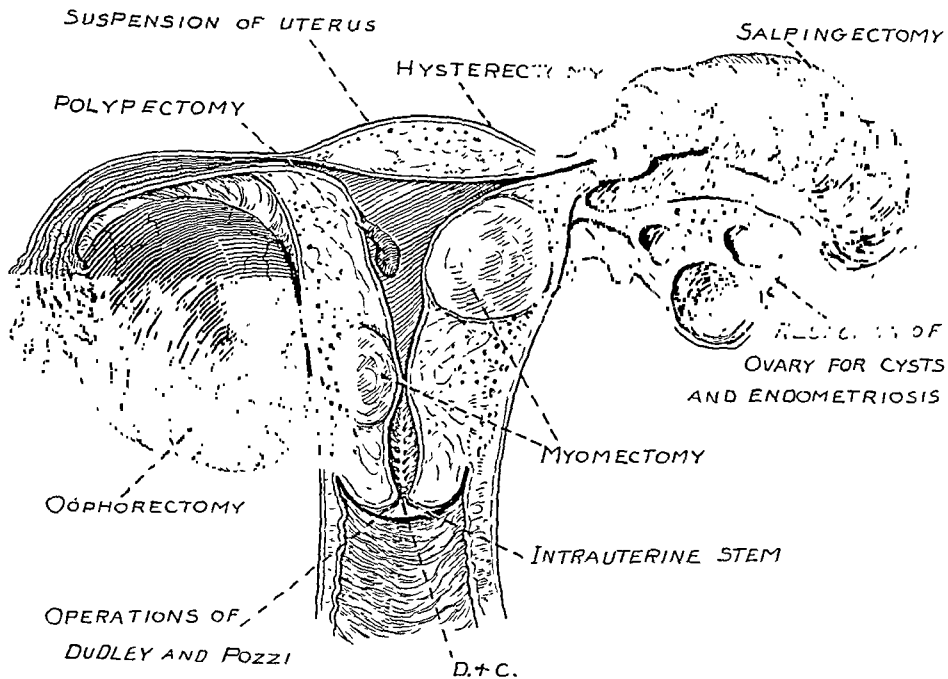


FIGURE 1. Composite Drawing Showing the Numerous Lesions That Cause Dysmenorrhea and the Various Surgical Measures That Are Employed in Their Treatment.

administration of analgesic drugs. Some of the newer antispasmodic drugs, by relaxing the uterine muscle, have proved of benefit, and in a certain group, hormones, notably progesterone, have been of value.

In severe cases and in those in which conservative therapy has failed, it frequently becomes necessary to resort to surgical measures. In primary dysmenorrhea thorough dilatation of the cervix, under anesthesia, usually brings relief, sometimes for a number of months and sometimes permanently. This is probably the oldest procedure in use, and years ago it was followed by curettage. Since then, however, it has been determined that it is the dilatation of the cervix rather than the removal of the endo-

metrium that is responsible for the improvement. The plastic operations of Dudley and Pozzi, designed to enlarge the external os of the cervix, were based on the theory that the cause of dysmenorrhea is mechanical. An annoying leukorrhea often followed this procedure however, and in many cases gynecologists have had to reconstruct the cervix to as near its original condition as possible in order to overcome this abnormal secretion.

It is in primary dysmenorrhea that presacral neurectomy or resection of the superior hypogastric plexus finds its greatest field of usefulness. The results are frequently dramatic, since it is not uncommon for young women who have been crippled each month by dysmenorrhea to menstruate without discomfort after this therapeutics. Because of the striking results there is the danger of being led

*Presented at the one hundred and sixty-third meeting of the Massachusetts Medical Society, Section of Obstetrics and Gynecology, May 24, 1944.

†Professor of gynecology, Tufts College Medical School, surgeon-in-chief, Department of Obstetrics and Gynecology, Carney Hospital; director, American Board of Obstetrics and Gynecology.

by one's enthusiasm to perform this operation on those who might be relieved by conservative measures. It should be resorted to only in those cases in which all other methods have failed, and should be reserved for the so-called "spastic" or uterine form of dysmenorrhea, a condition in which the patient experiences severe cramps. It has but little value in dysmenorrhea of ovarian origin.

Secondary dysmenorrhea is pain at the time of menstruation when certain pathologic lesions exist in the generative and adjacent organs. By the surgical ablation of the pathologic process concerned, menstruation may become nearly or entirely painless. Thus, in the presence of myomas that cause pain by the distortion of the uterus and by irregular contractions, in an attempt to expel blood clots, myomectomy or the enucleation of the tumors may result in marked improvement. The excision of endometrial polyps may give similar results, and ablation of the ovaries for ovarian cysts may be responsible for the cessation of menstrual pain.

It is a recognized fact that acquired dysmenorrhea is almost always due to endometriosis of the external variety, in which condition the ovaries are involved in the process. Relief of menstrual pain may be obtained by the resection or ablation of the ovaries, depending on the extent of the disease. Salpingophorectomy, unilateral or bilateral, may have to be resorted to for endometriosis and for chronic pelvic inflammatory disease in the form of adhesions, hydrosalpinx or chronic pyosalpinx. The last intervention may be performed independently or in association with hysterectomy. In such disorders as uterine myomas and adenomyosis, — also known as internal endometriosis, — hysterectomy, fundic, subtotal or total, with or without the ablation of the adnexa, may have to be employed. In corpus carcinoma the total removal of the uterus and its adnexa is the operation of choice. Since the manage-

ment of the above-named lesions, which are accompanied by painful menstruation, requires the removal of the uterus or ovaries, or both, thus bringing about the cessation of menstruation, it is obvious that the patient will be relieved of dysmenorrhea.

A number of years ago dysmenorrhea was attributed, in a large measure, to the retroposed uterus and was treated by dilatation and curettage and suspension of the uterus. Uterine suspension nowadays is not so frequently performed as it was in the past. When, however, a retroposition is discovered during a presacral neurectomy, the abdomen being open and the pelvic organs being accessible, the position of the uterus is usually corrected at the same time. The pain occasioned by mechanical disturbances of the vermiform appendix, as found in the retrocecal appendix and the distorted appendix due to adhesions, may be increased at the time of the catamenia. Lysis of the adhesions and an appendectomy frequently help the condition. Similar results may be obtained by attending to the lesions of the ureters, which appear as strictures, calculi and hydroureter. Diseases of the sigmoid and rectum, whether neoplastic, inflammatory or due to endometriosis, which may also cause increased pain at menstruation, demand proper surgical attention, and this secondarily effects improvement in or a cure of the dysmenorrhea. In membranous dysmenorrhea, in which a cast of the endometrium is thrown off with each menstruation, beneficial results have been obtained by curettage and a small dose of radium, about 200 to 250 mg. hr.

SUMMARY

The operative procedures in primary and secondary dysmenorrhea are discussed, and the operative procedures of the contiguous organs, the diseases of which are responsible for pain at the time of menstruation, are considered.

270 Commonwealth Avenue

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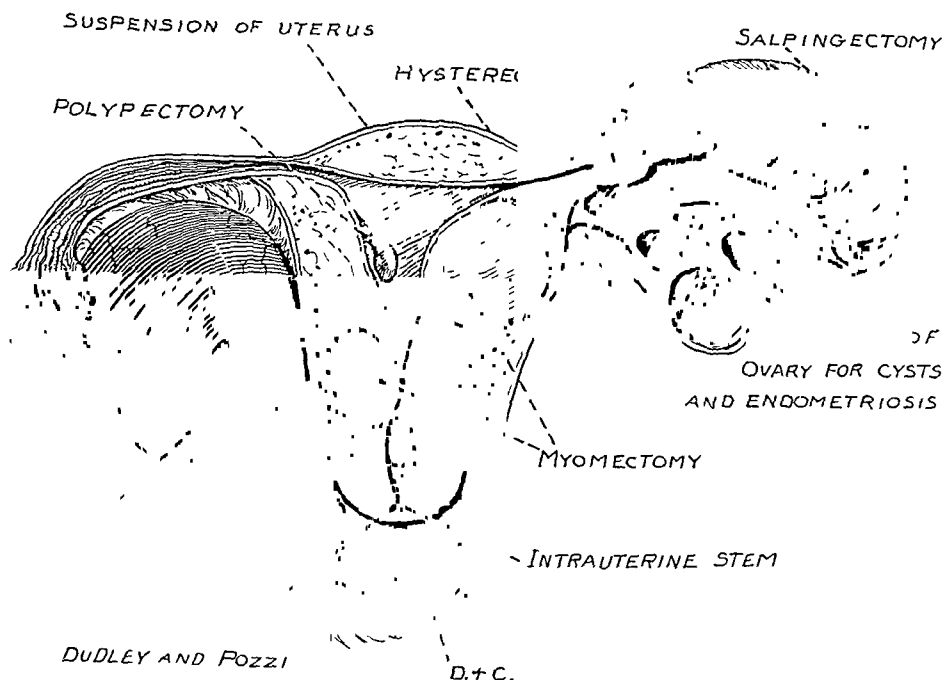


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this study. The distribution of these cases is shown in Table 1.

Merritt and Fremont-Smith¹ included 30 cases of metastatic brain tumor. The cerebrospinal fluid was 44 mg. per 100 cc. or less in 10 cases, 45 to 99 mg. in 15 cases, 100 to 199 mg. in 5 cases, and 200 mg. or more in 2 cases. Hare² determined the spinal-fluid protein in 6 cases of metastatic neoplasm. In 2 cases it was normal; in the other 4 it was 66, 77, 125 and 200 mg. per 100 cc., respectively. In Ayer's³ series, only one metastatic tumor was included, and in this case the protein of the lumbar cerebrospinal fluid was elevated.

The differential diagnosis of glioblastoma multiforme and metastatic neoplasms, which is often confusing owing to the fact that both these tumors develop signs and symptoms rather rapidly, is not helped by determining the spinal-fluid protein. In this series it was normal (40 mg. per 100 cc. or less) in only 19 and 9 per cent, respectively, and the comparative percentages for fluids with varying amounts of increased protein are very close, as shown in Table 1.

Table 2 indicates the separate findings in the 43 cases of metastatic tumor.

It is interesting to note that in 13 of the 26 cases in which the site of the primary lesion was found, it originated from the lungs. This certainly gives support to the rule that all brain tumor suspects should have chest x-ray examination as a routine procedure.

The fact that a neoplasm may be on the surface and even invade the ependyma of the ventricles without causing an elevation of the cerebrospinal-fluid protein is shown in Cases 2, 3 and 4. In all the cases with the greatest elevation of protein, however, the lesions were superficially located in

the cerebral hemispheres. Subcortical lesions are also capable of producing a marked elevation of protein, as shown in Cases 31, 33, 34 and 36. In the metastatic tumors, there was no apparent correlation between the type of primary tumor and the degree of elevation of protein.

The tendency of metastatic lesions to invade the supratentorial areas is brought out in this study, since there were only 6 patients with subtentorial metastatic neoplasms. Also, the protein was not markedly elevated in any of these, the highest level being 52 mg. per 100 cc. Hare² has found that primary subtentorial tumors, exclusive of acoustic neuromas, do not cause so great an increase in cerebrospinal fluid protein as do the supratentorial lesions. This is also apparently true of metastatic tumors.

SUMMARY

The average protein content of lumbar cerebrospinal fluid in 43 cases of metastatic brain tumors was 99 mg. per 100 cc.

Ninety-one per cent of the cases had a protein content greater than 40 mg.

The highest protein content was found in the cases with superficial cerebral metastases.

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THE CEREBROSPINAL FLUID PROTEIN IN METASTATIC BRAIN TUMORS

EDWARD W. SHANNON, M.D.,* AND CLINTON W. MORGAN, JR., M.D.†

BOSTON AND CLEVELAND

THE differential diagnosis between a primary and metastatic brain tumor is often difficult, were verified, either at operation or at post-mort examination. The fluid was obtained by lum

TABLE 1. Spinal-Fluid Protein in Cases of Brain Tumor.

TYPE OF TUMOR	39 OR LESS		40-99		100-199		200 OR MORE		ALL CASES	AVERAGE
	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage		
Metastatic tumors	4	9	23	54	12	28	4	9	43	99
Primary tumors:										
Astrocytoma	12	50	8	34	4	16	0		24	55
Glioblastoma multiforme	7	19	19	53	6	17	4	11	36	126
Meningioma	8	26	15	48	7	23	1	3	31	78
Medulloblastoma	3	60	1	20	1	20	0		5	70
Acoustic neuroma	0		1	8	5	38	7	54	13	272

and this study was made to determine whether the protein content of lumbar cerebrospinal fluid is puncture before any surgical procedures had be carried out. For comparison, the cerebrospinal

TABLE 2.

CASE No.	SEX	AGE	PRIMARY TUMOR	LOCATION OF METASTASIS	CEREBRO-SPINAL-FLUID PROTEIN mg /100 cc
1	F	43	Carcinoma of lung	Right parietal lobe; subcortical.	27
2	F	49	Medullary carcinoma of breast	Right frontal lobe; superficial. Right and left cerebellar hemispheres; superficial.	30
3	M	47	Bronchiogenic carcinoma (main-stem bronchus of left lower lobe)	Cerebellar hemispheres, pons, medulla, cerebrum and subependymal lining of both ventricles; superficial and deep.	30
4	F	39	Adenomedullary carcinoma of stomach (cardia)	Right and left frontoparietal lobes and cerebellum; superficial and deep.	30
5	F	65	Carcinoma	Right temporal bone and sphenoid ridge; extradural.	42
6	F	57	Adenocarcinoma	Left parietal lobe; subcortical.	42
7	F	37	Squamous-cell carcinoma of bronchus (left upper lobe)	Left frontoparietal lobe; subcortical.	45
8	F	38	Papillary adenocarcinoma	Left parietal lobe; subcortical.	45
9	F	54	Melanosarcoma	Right temporal and left frontal lobes; multiple superficial nodules.	45
10	F	49	Adenocarcinoma of bronchus (left lung)	Right frontal and temporal; deep. Left cerebellar hemisphere; superficial.	50
11	M	58	Epithelial neoplasm of glandular type (atypical glandlike structures lined by cuboidal or columnar epithelium)	Right cerebellar hemisphere; multiple nodules, deep and superficial.	50
12	M	55	Bronchiogenic carcinoma	Right frontoparietal lobe; superficial.	50
13	F	56	Adenocarcinoma of colon (carcinomatous degeneration of polyp)	Cerebellum	52
14	F	57	Carcinoma	Right frontal lobe	58
15	M	46	Bronchiogenic carcinoma (left main-stem bronchus)	Left parietal lobe; superficial.	60
16	M	52	Malignant tumor (probably carcinoma)	Right sphenoid ridge	65
17	M	44	Bronchiogenic carcinoma	Left parietal lobe; subcortical	66
18	M	30	Melanosarcoma (skin of left leg)	Right frontotemporal lobe; deep.	67
19	F	56	Carcinoma of thyroid or hypernephroma	Right parietal lobe; deep.	67
20	M	62	Carcinoma	Left parietal lobe; subcortical.	69
21	M	40	Melanosarcoma (probably skin of right temple)	Right anterior parietal lobe; superficial.	70
22	F	49	Papillary carcinoma of right lung (bronchiolar epithelium)	Right parieto-occipital lobe; deep.	80
23	M	42	Carcinoma of lung	Both hemispheres; multiple small superficial nodules.	85
24	F	53	Carcinoma of breast	Right frontotemporal lobe; superficial.	87
25	M	55	Colloid carcinoma	Right occipital lobe; superficial.	91
26	M	38	Carcinoma	Left parietal lobe; subcortical	93
27	M	48	Carcinoma of cortex of left adrenal gland	Right parietotemporal lobe; deep	95
28	F	54	Carcinoma of lung	Right frontoparietal lobe; superficial.	105
29	M	48	Adenocarcinoma	Left frontoparietal lobe; superficial.	108
30	F	46	Papillary carcinoma	Left frontal lobe; superficial.	110
31	F	58	Melanosarcoma	Left frontal lobe; subcortical	111
32	F	51	Adenocarcinoma	Right parietal lobe; superficial.	126
33	M	58	Carcinoma	Right frontal lobe; subcortical.	130
34	M	34	Melanosarcoma (skin of shoulder)	Left frontal lobe; deep.	146
35	M	50	Bronchiogenic carcinoma (left lung)	Anterior fossa; extradural. Right occipital lobe; superficial.	162
36	F	40	Carcinoma	Right occipital lobe; subcortical	170
37	M	24	Adenocarcinoma	Right frontal lobe; superficial.	180
38	F	49	Carcinoma of gastrointestinal tract	Left parietal lobe; superficial.	186
39	M	60	Carcinoma	Left frontal lobe; superficial.	216
40	M	34	Epidermoid carcinoma		242
41	F	64	Papillary adenocarcinoma		261
42	M	63	Adenocarcinoma of lung	Left frontal lobe; superficial.	311
43	F	58	Carcinoma of lung (right upper lobe)	Multiple small lesions disseminated through subarachnoid space; multiple small disseminated lesions. Temporal lobe; large superficial mass.	

an aid in differentiating these two conditions. All the 43 cases of metastatic brain tumor in this series

*Formerly, resident in neurosurgery, Massachusetts General Hospital, Boston

†Fellow in surgery, Cleveland Clinic, Cleveland.

fluid protein of an unselected series of verified primary brain tumors, including astrocytoma, glioblastoma multiforme, meningioma, medulloblastoma and acoustic neuroma, was carried in

this study. The distribution of these cases is shown in Table 1.

Merritt and Fremont-Smith¹ included 30 cases of metastatic brain tumor. The cerebrospinal fluid was 44 mg. per 100 cc. or less in 10 cases, 45 to 99 mg. in 15 cases, 100 to 199 mg. in 5 cases, and 200 mg. or more in 2 cases. Hare² determined the spinal-fluid protein in 6 cases of metastatic neoplasm. In 2 cases it was normal; in the other 4 it was 66, 77, 125 and 200 mg. per 100 cc., respectively. In Ayer's³ series, only one metastatic tumor was included, and in this case the protein of the lumbar cerebrospinal fluid was elevated.

The differential diagnosis of glioblastoma multiforme and metastatic neoplasms, which is often confusing owing to the fact that both these tumors develop signs and symptoms rather rapidly, is not helped by determining the spinal-fluid protein. In this series it was normal (40 mg. per 100 cc. or less) in only 19 and 9 per cent, respectively, and the comparative percentages for fluids with varying amounts of increased protein are very close, as shown in Table 1.

Table 2 indicates the separate findings in the 43 cases of metastatic tumor.

It is interesting to note that in 13 of the 26 cases in which the site of the primary lesion was found, it originated from the lungs. This certainly gives support to the rule that all brain tumor suspects should have chest x-ray examination as a routine procedure.

The fact that a neoplasm may be on the surface and even invade the ependyma of the ventricles without causing an elevation of the cerebrospinal-fluid protein is shown in Cases 2, 3 and 4. In all the cases with the greatest elevation of protein, however, the lesions were superficially located in

the cerebral hemispheres. Subcortical lesions are also capable of producing a marked elevation of protein, as shown in Cases 31, 33, 34 and 36. In the metastatic tumors, there was no apparent correlation between the type of primary tumor and the degree of elevation of protein.

The tendency of metastatic lesions to invade the supratentorial areas is brought out in this study, since there were only 6 patients with subtentorial metastatic neoplasms. Also, the protein was not markedly elevated in any of these, the highest level being 52 mg. per 100 cc. Hare² has found that primary subtentorial tumors, exclusive of acoustic neuromas, do not cause so great an increase in cerebrospinal fluid protein as do the supratentorial lesions. This is also apparently true of metastatic tumors.

SUMMARY

The average protein content of lumbar cerebrospinal fluid in 43 cases of metastatic brain tumors was 99 mg. per 100 cc.

Ninety-one per cent of the cases had a protein content greater than 40 mg.

The highest protein content was found in the cases with superficial cerebral metastases.

The patients with supratentorial metastases had a higher protein content than did those with subtentorial lesions.

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MEDICAL PROGRESS

TUBERCULOSIS

JOSEPH D. WASSERSUG, M.D.*

SOUTH BRAINTREE, MASSACHUSETTS

TUBERCULOSIS is a disease of innumerable ramifications; its many branches reach out from medicine and the allied sciences into the distant realms of sociology and law. Significant as all these ordinarily are, in time of war the main interest is in its great military importance.

TUBERCULOSIS, WAR AND POSTWAR

Tuberculous Rejectees

Last year special emphasis was placed on the ways and means that had been designed to keep tuberculosis out of the armed services.¹ Now, after three years of war, attention is shifting from case finding in inductees to the proper handling of tuberculous rejectees and veterans.

Although the follow-up of men rejected for tuberculosis varies in some details throughout the country, the general principles followed are fundamentally alike everywhere. Registrants disqualified for military service because of tuberculosis become, to a great extent, the responsibility of public-health officials, and their cases are submitted for study and review by competent authorities. Such follow-up is necessary since the degree of activity of a chest lesion cannot be determined from a single x-ray film. In fact, a definite diagnosis of tuberculosis cannot be made from a single roentgenogram. Hence, follow-up enables one to sort out the tuberculous from the nontuberculous, and the active from the inactive or arrested. The programs adopted by Chicago^{2, 3} Wayne County, Michigan,⁴ and Massachusetts⁵ have recently been discussed.

In Chicago, the Medical Advisory Board in conjunction with the Municipal Tuberculosis Sanitarium determines the disposition of cases rejected for tuberculosis. Of 1907 men with pulmonary tuberculosis seen in Chicago, 1279 were finally classified as 4F and 628 as 1A. Of the total number, 1431 cases (75.4 per cent) had never been previously reported to the Board of Health—a striking demonstration of the value of this type of case finding. On further study by the Collapse Therapy Clinic, 429 were selected as prospective candidates for treatment, and of these, 59 are now receiving pneumothorax.

In Massachusetts, rejectees for pulmonary diseases are first reported to the State Department of Public Health, and are subsequently referred to local

boards of health for further clinical and laboratory study. Practically all the rejectees are eventually examined in clinics conducted by the city, county or state. Of 2270 men so studied, 1795 (79.0 per cent) were rejected for pulmonary tuberculosis, 1672 of them with the reinfection type of disease. Complete follow-up was obtained in 1125 cases, and the diagnosis of reinfection-type disease was confirmed in every case. Of 395 men rejected as "pulmonary suspects," 160 received further study, and of these 86 were found to have tuberculosis. Important, though less striking than the Chicago demonstration, was the fact that two thirds of the cases of pulmonary tuberculosis that were discovered had never been reported to boards of health. Besides, 60 per cent of the cases were believed to be in need of immediate hospitalization. Thus, follow-up returns some men to the Army and sends others to sanatoriums or clinics for therapy.

Tuberculous Veterans

In spite of the many safeguards that have been set up to keep tuberculosis out of the armed services, it is disconcerting to learn that, up to the present, discharges from the Army because of this disease number approximately 10,000.⁶ Freer⁷ has estimated that 35 of every 10,000 men accepted for service have minimal, scarred or arrested lesions, and attributes some of the mistakes that have been made to inexperience, haste and fatigue of the examiners.

Myers,⁸ in a critical review, further analyzes the reasons for the failure to detect all cases of tuberculosis on induction into military service. Listed among the salient points are omission of x-ray examination of about 1,000,000 men who were first inducted, the use of the 4-by-5 inch or 35-mm. film instead of the 14-by-17-inch film, and the fact that even the best films cannot detect every case of tuberculosis. Myers stresses the role that could have been played by tuberculin testing of inductees and laments its exclusion from routine induction examinations. His original paper deserves careful reading.

There is, nevertheless, some reason to believe that the number of discharges for tuberculosis will soon show a progressive decline, and the figures from the Navy⁹ and from the Army Air Center at Nashville¹⁰ lend encouragement to this viewpoint. Men examined for air-crew training at this center are between eighteen and twenty-six years of age,

*Assistant physician, Norfolk County Hospital

and all have been in the Army for varying periods up to two and a half years. Examination of this group by the photoroentgen method revealed that the percentage incidence of tuberculosis in the first 32,000 was 0.207 per cent, in the second 32,000 0.169 per cent, and in the third only 0.120 per cent. In the last 10,000 examinations, indeed, it was less than 0.050 per cent. It is of some interest, too, that of the active cases of tuberculosis discovered, 112 were in the minimal stage, 10 were moderately advanced, and only 2 were advanced.

The Veterans' Administration is making every effort to absorb the load of new cases of tuberculous victims who have been discharged from military service. Statistics computed as of January 31, 1944, disclose that a total of 6114 beds were available for tuberculous veterans.¹¹ Under the so-called "G. I. Bill of Rights," plans were developed to provide an additional 3500 beds,¹² and this project has already received presidential approval.¹³

Unfortunately, tuberculosis among veterans is but little controlled by the availability of hospital beds or the expenditure of huge sums of money. Dublin¹⁴ points out that financial arrangements to veterans are such as to have had "the unfortunate effect of providing an incentive to many men to discontinue hospital treatment and to attempt a cure at home." In spite of the many millions of dollars that are being spent, the experience of veterans' hospitals has been unfavorable. For example, in 1942 less than 2 per cent of the patients were discharged as arrested. Hospitalization was considered incomplete in more than half the cases.

The reason for this alleged "deplorable situation," according to Dublin,¹⁴ is that veterans come and go as they please. Some have had as many as twenty-four different admissions; six to eight admissions is a commonplace occurrence. Yet the consequences of this indifference to treatment are far reaching. "The discharge of men," says this author, "before they are cured has left its toll on the entire country." Obviously, laws pertaining to veterans' benefits must be modified if tuberculosis among them is to be controlled.

The attitude of World War II veterans toward tuberculosis can arouse nothing but pessimism. Wolford¹⁵ reports that of 2275 such veterans treated for active pulmonary tuberculosis, approximately 31 per cent had left against medical advice before treatment was completed. Dublin¹⁴ writes, "There is already evidence that all is not well with the new tuberculosis victims, and that they are showing the same restlessness, the same abandonment of hospital care." An understanding of the dangers and seriousness of tuberculosis appears to be sadly lacking in too many servicemen. Altogether too often the term "tuberculosis" is regarded as being synonymous with a "short, pleasant vacation in the mountains."

United States Public Health Service

The establishment of a Division of Tuberculosis Control in the United States Public Health Service on July 6, 1944, may be "one of the most important steps yet taken toward the ultimate control of this disease."¹⁶ For this reason Section 2 of the bill¹⁷ under which this division was founded is quoted in detail.

Section 2. To enable the Surgeon General of the Public Health Service (1) to make studies, investigations, and demonstrations with respect to developing more effective measures of prevention, treatment and control of tuberculosis; (2) to assist through state health authorities, by grants as otherwise provided in this act, states, counties, health districts, and other political subdivisions of states in establishing and maintaining adequate measures for the prevention, treatment, and control of tuberculosis, including construction, maintenance, and operation, and the training of personnel for state and local health work; (3) to control the spread of tuberculosis in interstate traffic; and (4) to meet the cost of pay allowances, and traveling expenses of commissioned officers and other personnel of the Public Health Service detailed to assist in carrying out the purposes of this act, and for administration of this act, there is hereby authorized to be appropriated for the fiscal year ending June 30, 1945, a sum of \$10,000,000 and for each fiscal year thereafter a sum sufficient to carry out the purposes of this act.

In several articles, Hilleboe^{16, 18, 19} has elaborated on the purposes of the Division of Tuberculosis and has reviewed some of its accomplishments. The objectives of an adequate control program, he insists, must include mass x-ray examination (eventually, of the entire population), follow-up of discovered cases, isolation of open cases, treatment for active cases, periodic check-up, health education, research and financial aid to the afflicted. For the first step — mass roentgenography — the Public Health Service has available ten transportable units, some of which are equipped with the new photoelectric timer — a device that simplifies x-ray procedure by eliminating the necessity for measuring each subject's chest.

Industrial areas and large cities are the chief targets of the United States Public Health Service at the present time. Of 778,496 war workers examined by photofluorography up to May 31, 1944, approximately 1.0 per cent were found to have tuberculosis, and in two thirds of these cases the disease was in the minimal stage. Hiebert²⁰ reports a survey of 21,427 persons conducted in Kansas with a unit borrowed from the United States Public Health Service. Attention was centered on persons in war industries and "critical areas," and definite reinfection tuberculosis was found in 0.5 per cent. These figures are comparable to those of Massachusetts, where an x-ray survey of 28,190 persons in thirty-nine industrial companies revealed 352 cases of pulmonary tuberculosis, 114 of which were probably active.²¹

Hospital Personnel

It is common knowledge that medical students, nurses and others who assist in the care of tuberculous patients are exposed to a definite risk of

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dramatic cure for tuberculosis. Often by innuendo, less frequently by misstatement, preliminary in vitro or guinea-pig experiments have been presented as clinical successes. Usually these alleged "cures" depend on the discovery of a new "wonder" chemical or so-called "protective" vaccine. Chemicals and vaccines are being developed, but progress in this direction is slower and less certain than the laity is led to believe.

The chemical compounds of greatest promise are the sulfones. The parent drug, 4,4'-diaminodiphenylsulfone, is a potent agent for combating tuberculosis in guinea pigs,³⁶ but its toxicity limits its clinical application. Derivatives are therefore being synthesized in an attempt to obtain more suitable compounds for therapeutic use. The two derivatives that have received the greatest amount of study are promin (sodium *p,p'*-diaminodiphenylsulfone-*N*, *N'*-didextrose sulfonate) and diasone (disodium formaldehyde sulfoxylate, 4,4'-diaminodiphenylsulfone).

Three reports emphasize the value of promin in experimental tuberculosis in guinea pigs. In one group of tests, a favorable therapeutic effect in these animals was noted even though treatment was delayed for six weeks and the promin was given only in alternate weeks.³⁷ In another series of experiments, the average survival time of the treated animals was twice as long as that of untreated guinea pigs.³⁸ If the guinea pigs were first vaccinated, the subsequent administration of promin caused an even greater inhibition in the progress of the disease than occurred in the nonvaccinated animals.³⁹

Clinically, promin is not considered to be a particularly potent curative agent against human tuberculosis.⁴⁰ At the Wisconsin State Sanatorium, 27 patients with poor prognosis were given from 0.4 to 1.2 gm. of promin daily by mouth for a nineteen-month period. The status of 16 patients was ultimately evaluated; the improvement noted was greater than would otherwise have been expected. In another group of 36 adequately treated patients, marked improvement was observed in 7 and moderate improvement in 5.⁴¹ The authors of this report conclude, "Prolonged administration of promin orally is clinically feasible . . . [and makes] more extensive and more exactly controlled observations highly desirable." They stress the point that human beings, unlike guinea pigs, have a high degree of natural resistance to tuberculosis and are usually in need of but little aid in order to turn a losing fight against this disease into victory. When the fight is against tuberculous meningitis, however, promin has proved to be without any beneficial result in either prolonging or maintaining life or altering the course of the disease.⁴²

The clinical use of diasone has been discussed in some detail by Petter,⁴³⁻⁴⁵ who fed the compound to 100 volunteers and analyzed the results of treat-

ment in 44 of them. Diasone, it was concluded, is not an ideal chemotherapeutic agent but is to be regarded as a useful adjunct to other treatments. No correlation was discovered between the blood level of diasone and the clinical course. Toxic reactions were not infrequent but were not marked or irreversible. On the other hand, one very severe dermatitis was reported in another series of 63 cases.⁴⁶ Jellinek⁴⁷ found no useful effect from diasone in 15 cases of extrapulmonary tuberculosis.

A significant addition to the growing list of chemotherapeutic agents is promizole (4,2'-diaminodiphenyl-5'-thiazolesulfone).^{48, 49} It is apparently the least toxic of the therapeutic chemicals and is comparable in its effectiveness for guinea pigs to promin and diasone. Experimentally it is administered in daily doses of 200 to 250 mg., and favorable effects can be noted even in guinea pigs that have been inoculated ten to fourteen weeks earlier. Because of its low toxicity, it has been given orally to 56 patients in daily doses of 10 to 16 gm., but insufficient time has elapsed for evaluation of the results. A two-year-old child who presumably had tuberculous meningitis was treated with promizole and recovered,⁵⁰ but the diagnosis was not established with bacteriologic certainty and the result of a tuberculin test was not reported.

Among other compounds that have been tested for their bacteriostatic or bactericidal action on tubercle bacilli are certain naphthoquinones⁵¹ and stilbestrol.⁵² The latter exhibits a surprisingly strong bactericidal action in vitro. Penicillin and penicillium extracts have, by and large, no effect,⁵³ but another mold, as yet unidentified, is reported as having a bacteriostatic action.⁵⁴

Practically all the workers in this field of chemotherapy recognize the difficulties that are encountered in evaluating any agent for therapeutic use in human beings. The need for large numbers of cases, carefully matched controls, bacteriologic proof of disease and the objective, impartial evaluation of its course is stressed by Hinshaw and Feldman.⁵⁵ Pinner,⁵⁶ on the other hand, believes that absolute-control experiments in human beings are an impossible attainment and that any therapeutic agent, to be satisfactory, must be decisive in its results or is doomed to eventual discard.

SURGERY

Lloyd^{57, 58} has initiated a one-man campaign that is destined eventually to put pneumonology on a broader, sounder basis. Two features of this campaign are especially noteworthy. The first — inclusion of a chest service in a greater number of general hospitals — is designed to bring treatment for tuberculosis closer to the many persons who cannot obtain this service conveniently at present. The second feature — a bronchoscope for every lung specialist — is a natural outgrowth of the increased

infection. Schultz²² cites the cases of 24 medical students, 8 of whom developed active disease. He presents evidence that this group was carelessly exposed, and goes on to suggest that medical school faculties include in their curriculums definite programs to teach students the technic of handling patients with infectious diseases and that facilities for such precautions be provided. Certainly it is as important for students to learn how to protect themselves against tuberculosis as it is to detect it.

A recent survey by the Royal College of Physicians²³ is also instructive for the hints it provides for controlling tuberculosis among nurses. Mantoux tests and x-ray examinations were performed on 3764 nurses shortly after their entry into training school. Study of tuberculosis morbidity in those whose x-ray films were clear on entry revealed that 33 cases had occurred in 452 nurses initially Mantoux negative, but only 43 cases in 2120 initially positive. The annual case rate was 7.4 per 1000 for Mantoux-positive nurses, in contrast to 18.8 per 1000 for Mantoux-negative ones. It is therefore apparent that the young nurse who is tuberculin negative must be given special care and that her exposure to tuberculosis should be kept at a minimum.

Childress²⁴ reviews his experience with 5039 employees at the Grasslands Hospital, a general hospital of 800 beds, 300 of which are for tuberculous patients. If these employees are divided into two approximately equal groups, exposed and unexposed, it is found that 39 (1.8 per cent) of the exposed and 6 (0.2 per cent) of the unexposed developed tuberculosis. All these 45 employees originally had negative x-ray films and were symptom free. In this study, the laboratory was found to be a serious source of danger, since 5 active cases were discovered in the laboratory, in addition to several cases in physicians who worked there. There is no doubt that in many instances protection to laboratory workers against tuberculosis is wholly inadequate.

Foreign Countries

Throughout the world intensified programs for the control of tuberculosis are already under way or plans for the future are being laid. Mass photofluorographic check-up in Saskatchewan, Canada, has proved to be such a practical success that it has been stated that no city or municipality is so small or so large that it cannot raise the cost of such a survey.²⁵ In Alaska, where less than 100 beds are available for 2500 tuberculosis cases, proposals are being considered for the construction of hospitals to provide at least 400 more beds.²⁶ In Rio de Janeiro,²⁷ where tuberculosis is the leading cause of death, with an estimated death rate for 1944 of 309 per 100,000 population, and in other South American countries,²⁸ mobile x-ray units are being used and hospital facilities are being extended.

Reports from Victoria, Australia, indicate an increasing death rate from tuberculosis, and a program has now been launched that includes provision for 2000 beds and roentgenologic examination of every child at the age of twelve.²⁹ In fact, postwar plans have been made for compulsory chest x-ray examination of every person.³⁰

Trends and Perspectives

The tuberculosis mortality in the United States for the years 1939-1941 has been statistically analyzed by Yerushalmy and his co-workers.³¹ The death rate continues to show a gratifying decline; in 1942 it was 43.1 per 100,000 population, whereas in 1943 it was only 41.9. In highly industrial areas, however, especially in the north-central and north-eastern states, an increase has been noted.³²

A series of articles has appeared on the important problem of the apparently adequately treated patient whose sputum is occasionally positive or contains rare bacilli. Stokes³³ points out, "It cannot be denied that many patients with only a few bacilli in the sputum can and do lead comfortable, useful and economically productive lives and do not infect other members of their households." He recommends that discharge of patients from sanatoriums be not solely determined by the status of the sputum, but that consideration be given to such factors as age, sex, resistance, economic status and occupation.

In a more recent review, the Pottengers³⁴ call attention to the fact that tubercle bacilli may be detected on rare occasions in so-called "converted cases" if tests are done often enough and an exacting technic of examination is used. They believe that not every patient with an infection of the lung with rare bacilli in his sputum is necessarily suffering from active disease. In their studies, there has not been a single case in which a contact exposed to these patients has developed progressive clinical tuberculosis. Before discharge, a patient must indicate from every aspect that his lesion is healed; the sputum is but one item in the over-all picture.

Willis,³⁵ in a general discussion, has wisely summed up the problem as follows: "It is the duty of the laboratory to find tubercle bacilli wherever it can and to report them when found; the duty of the clinician is to evaluate the situation." The presence of tubercle bacilli may establish the diagnosis, but its significance may be totally different where therapy, discharge, prognosis and epidemiological connotations are concerned. Willis believes that there is a growing attitude of reasonableness about discharging patients for whom all has been done that can be done and who still occasionally produce a few bacilli.

CHEMOTHERAPY

During the past year, self-styled "science writers" have surpassed themselves in beguiling the public with a fleeting succession of hopes for a quick and

by Judd⁶⁶ for closing residual cavities following thoracoplasty. By an operative maneuver that he calls "lung mobilization and fixation," there is created a positive and forceful pressure on the cavity, and even some tension cavities can be closed by this method. With as trying a surgical problem as the tension cavity, it is good to have more than one method of approach.

A paper by Medlar and his associates⁶⁷ should prove of some aid in the surgical handling of chest diseases, since it provides for more accurate roentgenologic localization of lesions in relation to the pulmonary lobes. By employing an ingeniously constructed artificial thorax, they have obtained satisfactory roentgenograms of the interlobar septums in a variety of different positionings. They have thus devised a scheme in which the fourth and sixth costovertebral junctions serve as landmarks and by which the lobar distribution of the pulmonary disease can be readily recognized roentgenologically.

VITAMINS

The complex relation of vitamins to tuberculosis has many components, but there are two aspects that must not be confused with each other and must be discussed independently. The first is largely a problem in biochemistry, since it concerns the detection and the measurement of extent of vitamin deficiencies in tuberculous patients. The second is entirely a therapeutic problem, since it deals with the administration of vitamins for the correction of nutritional deficiencies and for the treatment of tuberculosis or its complications. To phrase the problem somewhat differently: Do vitamin deficiencies occur in tuberculosis, and if so how much can be gained by vitamin therapy? Unfortunately, a survey of the literature yields only incomplete answers to both questions at the present time.

The unqualified statement can be made that multiple vitamin deficiencies do occur in some tuberculous patients. This point has been established with reasonable certainty in spite of the facts that so-called "normal" vitamin levels are often established arbitrarily⁶⁸⁻⁷⁰ and that assays of a given patient's diet may be untrustworthy.⁷¹

Getz and his co-workers⁶⁸⁻⁷⁰ have discovered vitamin A deficiencies both by dark-adaptation tests and by blood-level estimations and, as might be expected, the deficiency of vitamin A is roughly proportional to the extent of tuberculous involvement. Breese and his associates⁷² fed measured amounts of vitamin A to 29 tuberculous patients, estimated its blood levels at given intervals thereafter, and found that in normal controls the rise of vitamin A in the blood was twice that of tuberculous patients. While admitting wide variations in single cases, the authors infer that in tuberculosis vitamin A is poorly absorbed from the intestinal tract and suggest that in this disease the diet be above average for vitamin A. An opinion has also

been expressed that tuberculous diabetic patients are in special need of this vitamin, and a daily dosage of between 150,000 and 200,000 units has been recommended.⁷³

Tuberculous persons may also be deficient in vitamin C.^{73, 74, 75} From studies on Navajo Indians, Pijoan^{71, 74} has concluded that tuberculous patients require an intake of vitamin C at least twice as great as that of normal persons to maintain a fixed plasma level of 0.7 mg. ascorbic acid per 100 cc. Pijoan⁷⁴ states, "This does not mean that vitamin C is to be specifically used in the treatment of tuberculosis as a therapeutic agent but rather as an adjunct to maintain proper ascorbic metabolism compatible with effective body economy." This confirms earlier work in which 24 patients were given 100 to 200 mg. of ascorbic acid daily, and in which it was found to be of no value in the treatment either of tuberculosis or of its complications, such as hemoptysis.⁷⁵

Nutritional studies by Farber and Miller⁷⁶⁻⁷⁸ disclose that deficiency in niacin, thiamine and vitamin K may also occur. According to these authors, hypoprothrombinemia was found to exist in 33 per cent of nonbleeding and 53 per cent of bleeding patients. The prothrombin time could be restored to normal in the majority of cases by the parenteral administration of menadione, but in spite of restoration to normal, hemoptyses often continued. Massive hemorrhages, in fact, sometimes occurred in patients with a normal bleeding time. The authors believe that it has not been established that vitamin K stops pulmonary hemorrhages or influences the course of the disease. In small hemoptyses, as Levy⁷⁹ points out, vitamin K may help to control bleeding, but evaluation of therapy for hemoptysis is a most difficult and uncertain task.

The relation of the B complex of vitamins to tuberculosis is but poorly understood. Extremely ill patients with far-advanced tuberculosis have a multitude of clinically detectable nutritional deficiencies, and some of these, it is true, are due to avitaminosis. In these extremely sick and often moribund patients, tuberculosis behaves more like a malignant process than an infectious disease, and efforts to stem the wasting of the body almost invariably end in failure.

According to Farber and Miller,^{77, 78} more than 75 per cent of acutely ill patients show some evidence of avitaminosis B. For treatment they recommend a basic supplement of 90 gm. of brewer's yeast, 150 mg. of niacin, and 6 mg. of riboflavin in divided daily doses. In specific deficiency states, up to 600 mg. of niacin, 15 mg. of riboflavin and 50 mg. of thiamine may be given daily. The authors noted some improvement in approximately 85 per cent of the patients so treated, but whether this therapeutic regime has any effect on the outcome of the tuberculosis is not stated. My own experience⁸⁰ with thiamine as a stimulant of appetite in tuberculous

use of bronchoscopy for the diagnosis and treatment of lung diseases.

Endobronchial Tuberculosis

McConkey and Gordon⁵⁹ have stressed the fact that tuberculous stenosis of major bronchi can be diagnosed clinically with an accuracy approaching 100 per cent. The cardinal symptom is wheezing. The diagnostic sign is the presence of rhonchi, occasionally audible, more frequently palpable, usually in expiration, and loudest over the stenotic bronchi. In their series of 95 tuberculous patients there were 61 who during the course of their disease developed persistent sonorous rhonchi unrelieved by cough. In 58 (95 per cent), the diagnosis of bronchial stenosis was confirmed bronchoscopically.

Lloyd and Budetti⁵⁷ have presented a comprehensive account of bronchial tuberculosis based on their experience with 475 bronchoscopic examinations. From the etiologic standpoint, they believe that tuberculosis in the parenchyma of the lung is always accompanied by changes in the mucous membrane of the draining bronchus. From the therapeutic standpoint, they find that although in some cases bronchial ulcerations heal spontaneously, cauterization is never of any value. Bronchial disease interferes more or less with drainage from the parenchymal focus, and this interference may be aggravated by collapse measures, especially pneumothorax. Hence, it is important to ascertain the state of the bronchi before attempting any collapse therapy.

A recent paper by Stone⁶⁰ gives an excellent description of the clinical aspects of endobronchial tuberculosis. In addition to wheezing and rhonchi, the author points out that the presence of an opaque or unexpandable lung during the course of pneumothorax is strongly suggestive of an underlying bronchial stenosis. Pain or soreness in the sternal region is described as a symptom in 30 per cent of the cases. Other diagnostic hints that are indicative of bronchial disease include failure of a cavity to close by thoracoplasty and clinical evidence of tuberculous bronchiectasis.

It must be remembered, however, that not all bronchial stenosis is due to tuberculosis. A fairly definite syndrome, benign nontuberculous bronchial stenosis, has been described.⁶¹

Major Surgery

Much of the recent literature on lobectomy and pneumonectomy for tuberculosis has already been reviewed by Blalock⁶² and Strieder.⁶³ Both these surgeons wisely caution that the use of resection for pulmonary tuberculosis is still in a formative stage and urge that the indications be not too rapidly extended. Time, rather than large series of cases, is necessary before the role of resection can be properly evaluated.

On the basis of their vast experience with lobectomy and pneumonectomy, Overholt and Wilson⁶⁴ have reached the following tentative conclusions: the operations are not associated with any unusual technical problems; tuberculous bronchitis or a positive pleural fluid is not necessarily a contraindication, nor is activity in the resected lung or stable (arrested) disease in the contralateral lung. Of sixty-three resections performed by Overholt from 1934 to 1943, thirty-five were pneumonectomies and twenty-eight lobectomies. The chief indication for operation was the presence of multilobar, predominantly unilateral disease. In forty-five consecutive resections since January, 1942, only 2 patients had contralateral spread; 2 had empyema, but none had a persistent fistula. In this group there were 36 reasonable-risk patients, and the operative mortality among them was 5.7 per cent. Conversion of sputum, however, was obtained in less than 70 per cent of the patients.

The ideal method for treating large cavities that remain open in spite of intensive collapse measures has not yet been found, but the progress made in this direction by Vineberg and Kunstler⁶⁵ is encouraging. They describe a method for needling such cavities and obtaining direct manometric readings of the intracavitary pressure, and they recommend that this procedure be carried out on cavities larger than 2.5 cm. before any major measure for surgical collapse is attempted. Special instruments are used for this test, and precautions are taken against complications such as empyema. On the basis of pressure determinations, Vineberg and Kunstler find that tuberculous cavities fall into three categories: those with an open bronchus and atmospheric pressure, those with a closed bronchus and negative pressure and those with check-valve mechanism and positive pressure. The last group, that of "tension cavities," has always presented a most difficult therapeutic problem, for such cavities are but little affected by surgical collapse. Negative-pressure giant cavities, on the other hand, close readily with thoracoplasty. The writers point out that it is the indiscriminate use of intracavitary drainage that has brought this valuable method of treatment into disrepute. Transthoracic intracavitary suction drainage should be employed only when a tension cavity is present, since this is the only true indication for its use. By the judicious application of suction, such cavities are reduced to the size of a catheter and can then be readily closed by thoracoplasty. The authors have performed needling of cavities in 150 cases and suction drainage in 27, without a single complication of hemorrhage, empyema, spontaneous pneumothorax or air embolism. Their valuable paper should be read by all who attempt any major chest surgery.

Almost supplementary to the methods described by Vineberg and Kunstler⁶⁵ is the technic outlined

by Judd⁶⁶ for closing residual cavities following thoracoplasty. By an operative maneuver that he calls "lung mobilization and fixation," there is created a positive and forceful pressure on the cavity, and even some tension cavities can be closed by this method. With as trying a surgical problem as the tension cavity, it is good to have more than one method of approach.

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children has been disappointing. As for riboflavin, decision concerning its significance must be withheld at present, since there is evidence that in some circumstances it may not be a dietary essential.⁸¹

During the last few years, McConkey⁸² has urged that cod-liver oil and tomato juice be employed in the treatment and prophylaxis of intestinal tuberculosis. From his assembled statistics it is inferred that the decline in the occurrence of this complication was coincident with the increased sale of cod-liver oil and canned citrus juices and the increased use of these preparations in his sanatorium. Be this as it may, the role of vitamin D in tuberculosis is still obscure, and accurate knowledge of its behavior is almost entirely lacking. A brief but excellent discussion of the therapeutic use of vitamin D in tuberculosis has appeared,⁸³ and it should be read before a course of vitamin D therapy is planned for the patient.

MISCELLANEOUS TOPICS

Bacteriologic technic and problems. Rapid methods have been described for concentrating and staining sputum specimens for tubercle bacilli. Reliable concentrations can be obtained by using a 5.25 per cent solution of sodium hypochlorite (Clorox) as a digestant.^{84, 85} Staining of specimens can be performed effectively at room temperature by adding propylene glycol to the staining mixture.⁸⁶ These technics should prove valuable timesavers for those laboratories already harassed by the lack of trained technicians.

The exact status of fluorescence microscopy for the detection of tubercle bacilli is still under discussion. The physical principles that underlie the method should be understood by those who attempt to use it. Laboratory studies show that it is roughly on a par with the Ziehl-Neelsen method for sputum examinations, but on gastric concentrates twice as many positive cases can be detected.⁸⁷ According to Graham,⁸⁸ fluorescence microscopy will not be ready for general use until it has been evaluated under the most favorable conditions that can be afforded by the average laboratory.

Variation in the virulence of tubercle bacilli is a problem that often plagues those working in the fields of bacteriology or immunology. Label designations may be unreliable. An approximate index of the degree of virulence can be rapidly obtained by injecting a measured suspension of weighed bacilli into the ear vein of a guinea pig.⁸⁹ Other experiments indicate that *in vitro* measurements of virulence can be obtained by culturing acid-fast bacilli with graduated amounts of diphtheria antitoxin.^{90, 91} Whether diphtheria antitoxin has any therapeutic role is not known, but some laboratory and clinical research is being conducted that may provide an answer to this question.⁹²

Virulence can apparently be altered by the presence of other micro-organisms as well as by chemi-

cals. Streptococci inoculated into rabbits seem to enhance the virulence of tubercle bacilli simultaneously or previously injected.⁹³ Avirulent human tubercle bacilli, on the other hand, have a definite retarding action on the course of the disease when injected into guinea pigs together with virulent bacilli.⁹⁴

Ultraviolet irradiation. Lurie⁹⁵ has demonstrated that in known strains of rabbits ultraviolet irradiation reduces the incidence of air-borne tuberculosis. In one set of experiments, 11 of 15 animals (73 per cent) exposed to air-borne tuberculosis in a non-irradiated room developed tuberculosis, and the disease was fatal in 9 cases, whereas not a single rabbit in the irradiated room became ill. Rabbits of low resistance as well as those of high resistance are protected by high-intensity irradiation.

Pregnancy. From a study of 26 women with advanced tuberculosis who received collapse therapy before giving birth to one or more children, Cutler⁹⁶ concludes that if the diseased area is anatomically well collapsed, the patient is afforded considerable protection against spread of the disease. Conversely, in cases in which an unsuccessful collapse is obtained, the prognosis is poor.

Congenital heart disease. When congenital heart disease complicates tuberculosis, pneumothorax is often delayed for fear of placing too heavy a burden on the cardiovascular system. That this idea is erroneous is borne out by the studies of Auerbach and Stemmerman,⁹⁷ who studied 13 such patients, 7 of whom came to autopsy and 5 of whom had pneumothorax. They state: "In view of . . . the fact that our own patients succumbed to the pulmonary involvement rather than to failure of the defective cardiovascular system, active treatment of tuberculosis is recommended. Pneumothorax induced in 5 of our patients did not lead to congestive failure in any instance."

Pneumothorax and airplane travel. By and large, persons with pneumothorax (artificial or traumatic) should be cautioned against traveling by airplane. Two well-planned articles, one published in this country⁹⁸ and the other in England,⁹⁹ point out that the moderate altitudes (5000 to 12,000 feet), usually attained by commercial airplanes are sufficient to produce a pronounced increase in the size or pressure of a pneumothorax. The risk of air travel is especially great in the presence of recently active disease, adhesions or reduced vital capacity and shortly after refills. If a patient with artificial pneumothorax must undertake a flight, he should go just before a refill, not immediately after one. An altitude of 4000 feet is regarded as the uppermost limit of safety for traumatic pneumothorax cases.

Diagnosis of early tuberculosis. In the diagnosis of early tuberculosis, even the best roentgenograms may be deceptive, since the disease actually begins as a microscopic lesion and interpretation of the

x-ray film is based on the gross appearance. Medlar and his associates^{100, 101} have presented remarkable demonstrations of this fact from both the clinical and experimental standpoints. By exhaustive laboratory studies, these authors were able to demonstrate tubercle bacilli in 2 per cent of a group of patients whose x-ray films were regarded as negative. In a subsequent series of experiments with rabbits who were intravenously inoculated with bovine tubercle bacilli, lesions were produced that could be carefully controlled and studied. Among the many important conclusions derived from this research was the fact that for a lesion to give a shadow, an area at least the size of a primary lobule must be densely packed with disease.

Vaccination with the vole bacillus. First isolated in 1937, the vole bacillus is a slow-growing Mycobacterium, apparently a third type of fixed mammalian tubercle bacillus.¹⁰² It is highly pathogenic for the vole, causes localized lesions in other laboratory animals, is innocuous to fowls, and gives no evidence that it will produce progressive disease when inoculated into man. In the experiments described by Brooke and Day,¹⁰² viable vole bacilli, heat-killed vole bacilli and Calmette-Guérin bacilli were compared in their effectiveness for protecting guinea pigs against subsequently induced experimental human tuberculosis. The results demonstrate that under the conditions established in these experiments, viable vole bacilli are at least equal, and probably superior, to Calmette-Guérin bacilli in their immunizing properties.

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FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor*

BENJAMIN CASTLEMAN, M.D., Acting Editor

EDITH E. PARRIS, Assistant Editor

CASE 30521

PRESENTATION OF CASE

A sixty-two-year-old fireman was admitted to the hospital in collapse.

Two days prior to admission the patient visited the Out Patient Department because of dysuria and frequency. Rectal examination in the Urological Clinic showed a moderately enlarged, smooth, firm, nontender prostate, and catheterization revealed a residual of 330 cc. in the bladder. Because the procedure was rather traumatic, he was admitted to the Emergency Ward for two days, the stay being uneventful. Immediately following discharge, while stooping to tie his shoes, he began to sweat profusely and complained of severe precordial pain. While climbing some stairs immediately afterward he again broke out into a cold sweat, emitted a queer noise from his throat, which sounded to his wife

like a "death rattle," and, on reaching the street, vomited and collapsed. He was immediately admitted to the hospital.

The patient had been a known hypertensive for about five years, and had been complaining of dyspnea on climbing stairs, fatigability and slight ankle edema. He had taken digitalis off and on for two years. Seven months prior to admission he had visited the Nerve Clinic because of an attack of headache, vertigo, vomiting and memory loss lasting about two days and followed by a dull ache about the right ear, which was relieved by aspirin. At that time the blood pressure was 175 systolic, 100 diastolic. The heart was enlarged, with an accentuated aortic second sound, and an occasional premature beat was noted. Many moist rales were present at the lung bases. There was a constant tremor of the head and arms, which was said to have increased over a period of ten years.

The family history revealed that one brother had heart disease and another was confined in a mental institution. His mother had died at fifty-three of a "shock."

Physical examination revealed a dyspneic, deeply cyanotic man. There was an incessant tremor of the hands and head. Respirations were Cheyne-Stokes in type. Bilateral arcus senilis and retinal arteriosclerosis were present. There were sticky rales at the lung bases. The heart was enlarged, the left border being 2 cm. outside the midclavicular line. Auscultation revealed slow fibrillation, with the pulmonic second sound greater than the aortic; no murmurs were heard.

The temperature was 97.6°F., the pulse 76, and the respirations 20. The blood pressure was 110 systolic, 90(?) diastolic.

Examination of the blood revealed a red-cell count of 6,100,000, with 13 gm. of hemoglobin and a hematocrit of 62. The white-cell count was 15,600, with 82 per cent neutrophils. The urine had a specific gravity of 1.016 and a 0 to +++ test for albumin; the sediment contained 10 red cells, many

the right base. The left lung did not show this haziness. The heart was greatly enlarged in the region of the left ventricle. Examination three days later revealed marked increase in the pulmonary process (Fig. 1). The right lung was particularly dull, with numerous areas of increased density through which only little aerated lung could be seen. The hilar shadows and blood vessels were enlarged, and there was increased marking throughout the



FIGURE 1. *Roentgenogram of Chest.*

white cells and rare hyaline and granular casts per high-power field. The serum nonprotein nitrogen was 110 mg. per 100 cc., and the van den Bergh test was 0.5 mg. direct, and 1.2 mg. indirect.

On the night of admission the patient was restless and vomited several times. He was given oxygen, together with 0.19 gm. of quinidine sulfate every four hours, 0.1 gm. of digitalis a day, 0.25 gm. of sulfathiazole three times daily and paraldehyde for sedation. The following morning he vomited clear fluid containing a small amount of bright-red material. The pulse rate was 110, and he was sweating.

A portable roentgenogram of the chest revealed a hazy increase in density in the right chest that had a ground-glass appearance and was most marked at

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discontinued, since it did not appear to affect his status appreciably. He continued to fibrillate, and the lungs became almost clear to auscultation. The serum nonprotein nitrogen rose to 105 mg. per 100 cc., and the white-cell count, which had fallen to 9400, rose to 19,400. On the thirty-fifth hospital day he had a brief attack of shock, during which the blood pressure was unobtainable for a short period. He became increasingly confused, cyanotic and dyspneic and expired on the fortieth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. MAURICE FREMONT-SMITH: This patient was a sixty-two-year-old man with a family history of vascular disease who manifestly had hypertensive heart disease with failure and probably some coronary disease. On the other hand he came to the hospital because of urinary symptoms and was catheterized, 330 cc. of urine having been removed from the bladder. The prostate was not thought to be large by rectal examination. One cannot tell much about urinary obstruction by rectal examination; this patient manifestly had obstruction, and long-continued obstruction can cause elevation of the nonprotein nitrogen. He left the hospital after catheterization, had some sort of an acute episode with precordial pain and then collapsed.

I believe that any one of five things could have happened to him. He might have had a coronary thrombosis, and that is perhaps the first choice. He could have had a rupture of a dissecting aneurysm, since he was a known hypertensive. Against this is the fact that the pain was anterior rather than posterior. In dissecting aneurysm pain occurs chiefly in the back between the shoulder blades or lower. In coronary thrombosis there may be pain in the back between the shoulder blades, but if present it is always associated with greater pain anteriorly. He could have had a cerebral accident, which might have caused the state of shock but could not have accounted for the precordial pain. He could have had simply a change in cardiac rhythm. Sometimes that causes precordial pain, and in a man with a poor heart, such a change in rhythm, the onset of fibrillation, for instance, may cause collapse. He could have had a pulmonary infarct, since the circulation was poor. Of course I am influenced by the fact that they tied the femoral veins; someone must have thought that he had a pulmonary infarct. The cerebral accident, with headache, vertigo, vomiting and memory loss, I cannot explain except on the basis of small cerebral thromboses, which are part of the general picture of a bad vascular situation.

The systolic blood pressure was 175, but I am quite sure that it had been higher because he was already in failure. After he came into the hospital it was 110 systolic, 90 diastolic, and he was mani-

festly in shock. He had a red-cell count of 6,000,000 and a hematocrit of 52, which indicate either concentration from dehydration or, likelier, a chronic compensatory erythremia from anoxemia, the result of heart failure. The white-cell count of 16,000 may have been due to concentration or possibly to a response to a pulmonary infarct. The urine is interesting because at one time he had no albumin and because the nonprotein nitrogen came down to normal in the hospital; both these findings argue against an actual uremia in the sense of primary kidney disease. He may have had back pressure from the prostate, which would interfere with the function of the kidneys. He certainly could have had a rising nonprotein nitrogen with myocardial infarction, owing to insufficient circulation to the kidneys. The van den Bergh test was slightly elevated, probably as a result of chronic passive congestion of the liver. He was restless and vomited several times on admission. He was given oxygen, which is reasonable, quinidine sulfate to protect him against ventricular fibrillation, which is reasonable, and digitalis.

I want to say a word about the sulfathiazole. They gave it cautiously in exceedingly small doses, probably for the urinary infection. It may have been given because the patient was on constant drainage. I should like to know about that.

DR. JACOB LERMAN: Yes; that is correct.

DR. FREMONT-SMITH: One should be particularly careful in giving sulfonamides to elderly people with bad kidneys, remembering that one may get toxic symptoms, particularly anuria, with very small amounts of sulfonamides. In any case the main thing to remember is not to give treatment that may do harm. I am interested in an article on the toxic symptoms of sulfonamides by Vilter and Blankenhorn,¹ especially the discussion by Dr. David Lehr, who has carried out animal experimentation. Dr. Lehr states that if they give plenty of alkali, animals survive very large doses of sulfadiazine; they do not get into difficulty with the kidneys, and when they are killed, no pathologic changes are found. If, on the other hand, animals that have an obstruction in the pelvis or have developed crystals are given alkali, they die rapidly. If given plain water, they die from water intoxication. Under these conditions the tubules reabsorb all the fluid and no water gets into the collecting tubules. The medication that brought about the greatest benefit in cases with a deposit of crystals were salts, either sodium chloride or a mixture of sodium bicarbonate and ammonium chloride. Apparently, if one gives a large amount of electrolytes, reabsorption from the tubules does not take place and fluids are excreted through the kidney, thus washing out the sulfadiazine crystals; but plain water or sodium bicarbonate given at the time of obstruction is detrimental. If one is going to protect a patient against sulfonamide crystalluria, apparently one should

elevation being extremely high. R waves were absent in Lead CF₄. There was slight late inversion of the T waves in Leads 1 and CF₅. There were also two ectopic ventricular contractions in other leads on this first occasion. The second electrocardiogram (Fig. 2B), taken two days later, showed a distinct change except for the auricular fibrillation. The small Q waves in Lead 1 persisted, but there were almost no R waves in that lead, and small S

low in the three limb leads. There were no R waves in Leads CF₄ and CF₅, and the ST segments were elevated in both these leads, with low T waves. In the last record, taken two weeks after the third, the record in general resembled the previous one.

Because of the possibility that a pulmonary infarction had occurred, a bilateral superficial femoral-vein ligation was performed on the second hospital day. The patient's lips remained cyanotic, and the

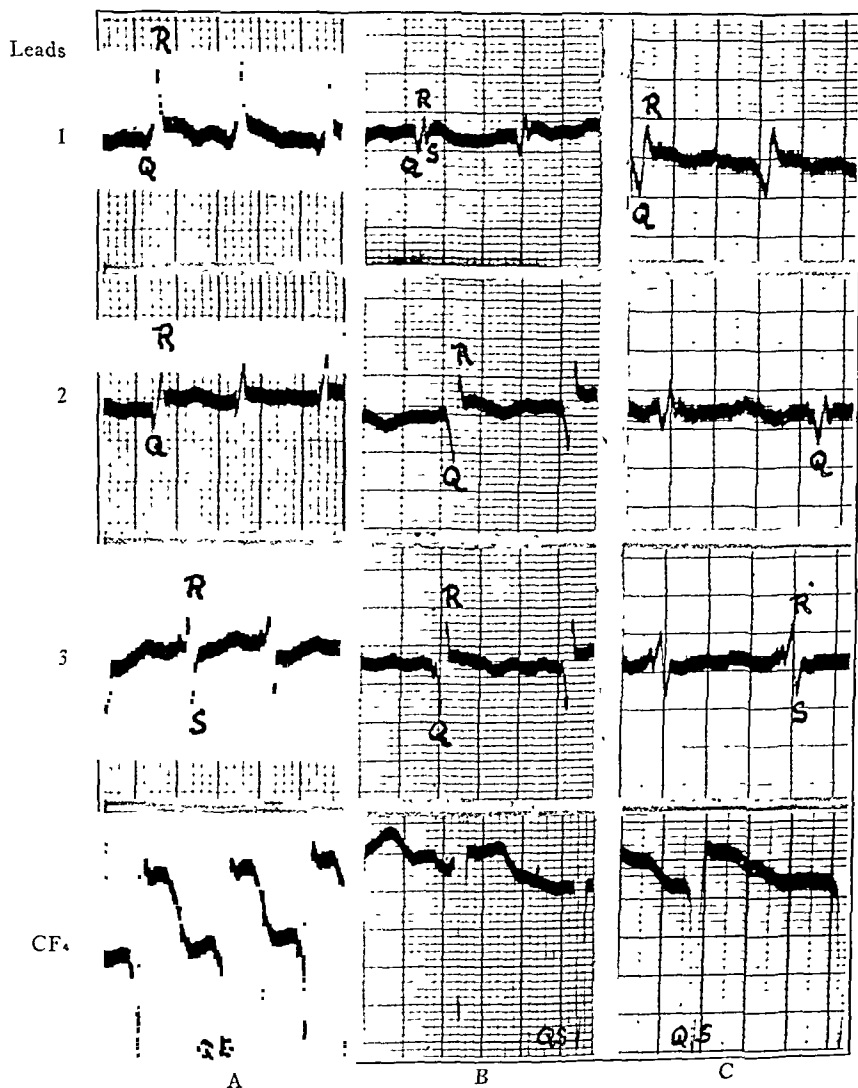


FIGURE 2. Electrocardiograms.

A was taken on the day of admission; B, on the third hospital day; and C, on the fifth hospital day.

waves had appeared. The T waves were slightly inverted. In Leads 2 and 3 there were distinct and striking changes: deep Q waves had appeared, the ST segments had become a little elevated, and the T waves were inverted. In the precordial leads the ST segments were within normal limits. In the third electrocardiogram (Fig. 2C), two days after that, there was an abrupt shift in the limb leads back toward the first record, in that there was no longer any Q wave in Lead 3, and Q wave in Lead 2 had become much smaller, and there was a deep wide Q wave in Lead 1. The T waves were flat to

neck veins moderately distended. On the third hospital day he complained of a "stitch" in the left chest anteriorly, just medial to the nipple, on coughing or on deep breathing. He gradually improved on a cardiac regimen augmented with oxygen. The serum nonprotein nitrogen gradually fell to normal, but the patient continued to have orthopnea, some dyspnea and moderate cyanosis. He showed a gradually increasing degree of confusion, with marked memory defect and lack of time orientation and insight.

On the twenty-sixth hospital day

gen. was

caused by an infarct and pulmonary edema. He certainly would have died immediately if the extensive lesion had been solely due to an infarct. Consequently we thought that the picture was partly caused by edema.

CLINICAL DIAGNOSES

Cardiac failure, with coronary heart disease.
Hypertension
Pulmonary infarct.
Uremia.

DR. FREMONT-SMITH'S DIAGNOSES

Hypertensive and coronary heart disease, with cardiac infarction.
Obstructing prostate (? uremia), with urinary infection.
Generalized and cerebral arteriosclerosis.
Pulmonary infarct.

ANATOMICAL DIAGNOSES

Coronary thrombosis, recent: left descending branch.
Myocardial infarct, recent: anterior wall.
Mural thrombus: left ventricle.
Thrombus occluding right pulmonary veins: left atrium.
Hemorrhage, severe: right lung.
Alveolar fibrosis: right lung.
Hydrothorax, bilateral.
Pericardial adhesion.
Chronic passive congestion with central necrosis of liver.
Nephrosclerosis, mild.
Renal infarcts.
Prostatic hypertrophy.
Urinary bladder hypertrophy, with trabeculation and pseudo diverticula.
Arteriosclerosis, severe, generalized.
Operation: femoral vein ligation, bilateral.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy showed an unusual condition. There was a thrombus of the descending branch of the left coronary that had produced a massive myocardial infarct in the anterior wall of the left ventricle, over which was a large mural thrombus (Fig. 3). In the left auricle was a ball-shaped thrombus, 3 cm. in diameter, which was well organized and only slightly adherent to the auricular endocardium but which could easily be pulled away leaving a not too ragged endocardial lining. This thrombus had completely plugged the openings of both right pulmonary veins, so that little blood was coming from the right lung. There was no extension of the thrombus into the veins.

The openings of the left pulmonary veins were normal. The entire right lung was dark, hemorrhagic and firm and weighed over 1000 gm., whereas the left lung was crepitant and weighed slightly under 400 gm. Certainly not much blood, if any, was coming from the right lung, which accounts for the marked contrast between the roentgenologic appearance of the right and the left lung. It is



FIGURE 3. Photograph of Heart.

intriguing to speculate how the occluding thrombus originated. There was a small and much more recent mural thrombus in the left auricular appendage that may have been the source. The occluding thrombus looked much like the mural thrombus over the ventricular infarct, but it would be rather farfetched to assume that a piece of it traveled against the current through the mitral valve into the auricle. It may have been produced merely by the auricular fibrillation.

DR. WHITE: Did the auricular myocardium look all right?

DR. CASTLEMAN: Yes; there was no infarction. We have to assume that the thrombus was there at the time of admission to the hospital because the change in the right lung was seen in the first film. Although the lungs in gross suggested infarction there were no emboli or microscopic evidence of infarction. The left lung showed slight chronic passive congestion. At first glance it looked like infarction, but all the alveolar walls were intact.

start the alkali before starting the sulfonamide; if the alkali is started later, it is not so valuable.

I shall say a word or two about paraldehyde. Paraldehyde is looked on as a safe drug, but Burstein² has reported 2 fatal cases, and by animal experimentation he found that with toxic doses animals die of right auricular dilatation. The difference between the effective dose and the toxic dose with paraldehyde is extremely slight. In psychotic patients with a good heart, paraldehyde seems to be a safe drug, but in a person with cardiac failure one should possibly think twice before giving a drug that produces fatal cardiac dilatation in animals.

Why did this patient vomit red material? Patients with chronic nephritis develop acute ulcer, and so do those with uremia. He may have had an ulcer, but it may have merely been evidence of chronic passive congestion in an old man who was vomiting.

I think that we might see the x-ray films at this time.

DR. LAURENCE L. ROBBINS: There is obvious enlargement of the heart, even though the film was not taken for the heart size, and a rather diffuse increased density throughout the medial portion of the right lung with some involvement at the base. In the first film there is nothing characteristic about the appearance. The second film (Fig. 1) shows a more diffuse process. The bronchi remain open, and the greater portion of the process appears to be within the lung. Certainly there is some fluid in the right pleural cavity, and a small amount in the left. One thing about it is that all the shadows appear to be more sharply defined than they were at the time of the previous examination.

DR. FREMONT-SMITH: Would you say that the findings are consistent with pulmonary infarcts?

DR. ROBBINS: If it is an infarct, it is a massive affair, and I should have to place the embolus in the main pulmonary artery.

DR. FREMONT-SMITH: Do you think that it is a diffuse bronchopneumonia?

DR. ROBBINS: I do not know. It does not look characteristic of anything. It could be consolidation throughout the lung, with bronchopneumonia as a terminal affair, but this film was taken some time before he died. So far as I am concerned it could be a massive infarct or a diffuse pneumonia, with a small amount of pleural effusion on each side.

DR. FREMONT-SMITH: That is certainly consistent with the diagnosis of pulmonary infarct.

DR. ROBBINS: If it is an infarct, it is the largest one that I have seen.

DR. FREMONT-SMITH: An infarct of that size should have been immediately fatal. I wish that Dr. White would discuss the electrocardiograms, which are beyond my depth. I should like to know whether the electrocardiograms differentiate pulmonary infarct and coronary disease. I should say

that this patient had coronary disease, whether recent or old I do not know.

DR. PAUL D. WHITE: The electrocardiograms are extremely interesting. One of the most significant findings is not the auricular fibrillation but the other disturbance of rhythm found on the first day, namely, the probable ventricular paroxysmal tachycardia which strongly suggests myocardial infarction or the toxic effect of digitalis. Furthermore, the variations in the QRS waves, ST segments and T wave in the limb and precordial leads are also particularly significant and confusing. The first (Fig. 2A) third (Fig. 2C) and fourth electrocardiograms are absolutely characteristic of the effect of anterior myocardial infarction, as shown by the Q waves in Lead I, the absence of the R waves in Leads CF₁ and CF₂, and the ST segment elevations in Leads I, CF₁, and CF₂. We might have expected, however more definite inversion eventually of the T wave in Leads I, CF₁, and CF₂, which did not develop during the time in which these electrocardiograms were taken.

The second electrocardiogram (Fig. 2B), taken two days after admission, is the one that is the most interesting because of the abrupt temporary but striking differences from the first and the later electrocardiograms. Here the findings suggest those either of posterior myocardial infarction or of an acute cor pulmonale superimposed on some effects of the anterior myocardial infarction. The deep Q waves, the inversion of the T waves in Leads 2 and 3 and the small S waves in Lead 1 make one think of a cor pulmonale. The effect is, in the main, temporary, and the T waves in Leads 1, CF₁, and CF₂ may have failed to become inverted in later records, owing to the increased pulmonary pressure. Thus, the electrocardiograms show a complicated condition either in the form of multiple involved myocardial areas or in the form of a combination of the factors of myocardial infarction and of acute cor pulmonale.

DR. FREMONT-SMITH: I think that this patient had hypertensive and coronary heart disease, with cardiac infarction and probably pulmonary infarction, obstructing prostate and urinary infection. There may have been a terminal bronchopneumonia as well; and there was, of course, generalized arteriosclerosis and cerebral arteriosclerosis.

DR. LERMAN: I should like to make a few comments in answer to some of the questions raised by Dr. Fremont-Smith. The mental state was probably due to anoxemia. The patient was always cyanotic and markedly orthopneic. I can visualize him tossing around in bed in a disoriented manner. The bizarre nitrogen fluctuations undoubtedly were due to the fact that he pulled out his catheter every so often. Whenever he did that, he became obstructed and the nitrogen values rose. I do not know the exact interpretation of the unusual x-ray changes, but as I recall it the explanation was that they were

progressively worse and were associated with weakness, anorexia and loss of weight. About nine months prior to entry, in spite of her increasing symptoms, the patient was married. Following marriage, she appeared to improve somewhat but soon developed a cold, associated with an exacerbation of her symptoms. She had lost 18 pounds since the beginning of her illness, dropping from 116 to 98 pounds, and because of increasing weakness she entered a community hospital. The red-cell count was said to have been 2,600,000. After five weeks of symptomatic treatment, augmented by transfusions, she was discharged considerably improved, the red-cell count having risen to 4,300,000. She was sent to a convalescent home, where she gained weight and strength. The diarrhea had practically ceased and there was no blood in the stools. One month later, about five and a half months before admission, she developed a sharp, stabbing pain in the right upper thorax just below the shoulder, made worse by respiration. The pain lasted about a week and was treated by diathermy. Shortly thereafter she developed severe bloody diarrhea and was again hospitalized. A sigmoidoscopic examination at that time was said to reveal "pinpoint ulcers that bled easily." She suffered severe abdominal pain, requiring morphine for relief. Four months before entry she was transferred to another hospital, at which time she was bleeding profusely by rectum and appeared almost in extremis. She complained of cough, which was accompanied by a small amount of white frothy sputum and chest pain, and was running a low-grade, undulating fever without chills. There was no hemoptysis. A roentgenogram of the chest revealed elevation of the right half of the diaphragm and increased density over the entire right lung; the latter was interpreted as being due to pleural effusion, but several taps were unsuccessful. The left chest was clear. A loop ileostomy was performed, and a spontaneous ileostomy developed proximal to the operative ileostomy two weeks later. In spite of the ileostomy, numerous transfusions and nearly 1,000,000 units of penicillin, the patient showed no improvement and had several major hemorrhages by rectum. About one and a half weeks before entry she had a sudden attack of dyspnea and cyanosis, with a temperature of 105°F., apparently following an injection of penicillin. The next day the temperature was 95°F., and she subsequently improved rapidly.

The patient was born in Oklahoma and had lived there until shortly before the onset of her illness. She had had three attacks of rheumatic fever at the ages of seven, nine and seventeen years, respectively, without apparent sequelae.

Physical examination revealed an extremely weak, lethargic, markedly cachectic woman. The skin was cold, dry and pale, with little subcutaneous fat. The skin around the ileostomy openings was inflamed, undermined and tender. The scars of several

decubitus ulcers were present. There was an infected area over the sternum, apparently the site of a bone-marrow infusion. The chest was small and sunken, with marked splinting on the right. The lower half of the right chest was dull to percussion anteriorly and posteriorly, and breath sounds over this area were diminished to absent. Elsewhere on the right the breath sounds were bronchovesicular with numerous coarse inspiratory rales. The left chest was clear. There was a rough apical systolic murmur obliterating the first sound. There were flexion contractures of both legs and slight clubbing of the fingers.

The temperature was 100°F., the pulse 90, and the respirations 25. The blood pressure was 80 systolic, 40 diastolic.

Examination of the blood revealed a red-cell count of 4,000,000, with 55 per cent hemoglobin, and a white-cell count of 9000, with 70 per cent neutrophils and 30 per cent lymphocytes. The urine was essentially negative. The blood serum nonprotein nitrogen was 21 mg. per 100 cc., the protein 4.9 gm., with an albumin-globulin ratio of 1.4, and the chloride 89-99 milliequiv. per liter. The van den Bergh test was 1.1 mg. per 100 cc. direct, and 1.8 mg. indirect. The prothrombin time was 38 seconds (normal, 18 to 20 seconds). A tuberculin test in a dilution of 1:1,000,000 was negative.

A roentgenogram of the chest (Fig. 1) revealed a miliary process scattered throughout both lung fields, with dense consolidation in the middle lobe on the right and evidence of some consolidation in the right lower lobe. The right half of the diaphragm was not clearly visualized. There appeared to be a cavity in the posteroinferior portion of the right lower lobe that was connected with a bronchus. The heart and mediastinum appeared to be in normal position, and the liver and spleen were enlarged.

The patient was given transfusions, infusions and penicillin. On the second hospital day she developed sudden dyspnea and cyanosis, with distended neck veins and many inspiratory rales and wheezes. The pulse was 120, and the respirations 35. Following the use of tourniquets, oxygen and Cedilanid she improved rapidly. The following day examination revealed moderate edema of the lower extremities. There was no engorgement of the neck veins. The point of maximum cardiac impulse was felt 2 cm. beyond the midclavicular line. The heart rhythm was regular, with a diastolic gallop. The second pulmonic sound was extremely loud, and there was a questionable mid-diastolic rumble at the apex. An electrocardiogram showed rather low T waves but nothing of definite diagnostic value. The patient continued to run a fever between 100 and 103°F. A spasm of coughing on one occasion was productive of a small amount of bloody sputum that was negative on smear for acid-fast organisms. She had several attacks of pulmonary edema similar

and the alveoli were filled with blood. The other striking thing in the right lung and not in the left was the presence of numerous areas of fibrosis within the alveoli (Fig. 4), a picture that Masson³ has described in rheumatic pneumonia. It occurred to me that perhaps these fibrous plugs should not be ascribed to rheumatic pneumonia but to pulmonary

to state that any electrocardiographic findings are pathognomonic, but we can almost surely say that prominent Q waves in Lead 1, especially when carried over to Lead 2, are rarely found in any condition other than anterior myocardial infarction. (If Lead 1 is upside down, owing to congenital dextrocardia, that is another thing.

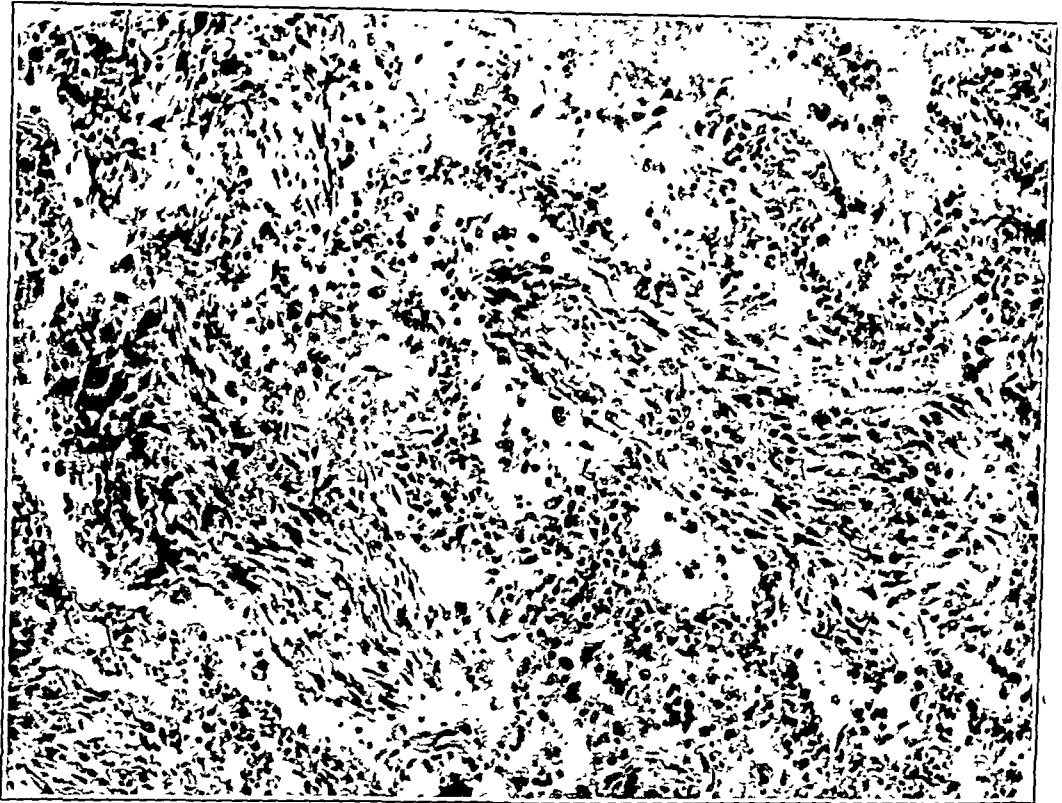


FIGURE 4. Photomicrograph of Lung Showing Intra-Alveolar Fibrosis.

hypertension, since they were not present in the other lung. We know that most rheumatic patients have mitral stenosis with pulmonary hypertension, and perhaps we have here a clue to the cause of so-called "Masson bodies." There were no hyaline membranes of the alveoli, another finding in some cases of rheumatic pneumonia.

DR. WHITE: Do you know of a similar case in the literature? I have never heard of one.

DR. CASTLEMAN: No.

Another finding was a hypertrophic and trabeculated bladder due to prostatic enlargement, with no evidence of distention of the renal pelves or pyelonephritis. There were a few renal infarcts, which must have been produced by emboli from the mural thrombus in the heart. There were also thrombi in the deep veins in the legs, but none of these could have reached the lungs because of the bilateral femoral-vein ligation.

DR. WHITE: I should like to make a further comment about the electrocardiograms. We hesitate

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CASE 30522

PRESENTATION OF CASE

A twenty-year-old married woman was admitted to the hospital with persistent diarrhea.

The patient was perfectly well until a year prior to admission, when she had an attack of "intestinal grippe," with abdominal pain, malaise and cough, which was productive of phlegm but not of blood. After a few days she again felt well. About two months later she first noted some red streaking at stool and had a mild diarrhea. A local physician was consulted, and she was treated for hemorrhoids, without effect. The diarrhea and bleeding became

persistent ulcerative lesion in the colon, definite evidence of pulmonary disease. The interpretation of the type of pulmonary disease is particularly difficult unless the density was greater than I assumed that it was; slight density over the entire chest is rather unusual if due simply to pleural effusion. The absence of a large pleural effusion seems to have been borne out by the fact that taps were unsuccessful. From that time until death the pulmonary disease increased rather steadily. Perhaps this is the best time to see the x-ray films.

that the patient probably had rheumatic heart disease with mitral involvement, a sequela of the three attacks of rheumatic fever. Whether or not the attacks of pulmonary edema that came on acutely on several occasions during the last few days of her life were related to the underlying cardiac disease is impossible to say. It would be unusual to have these symptoms if cardiac failure were secondary to the pulmonary involvement. The question whether a rheumatic myocarditis was also present at that time cannot be answered,

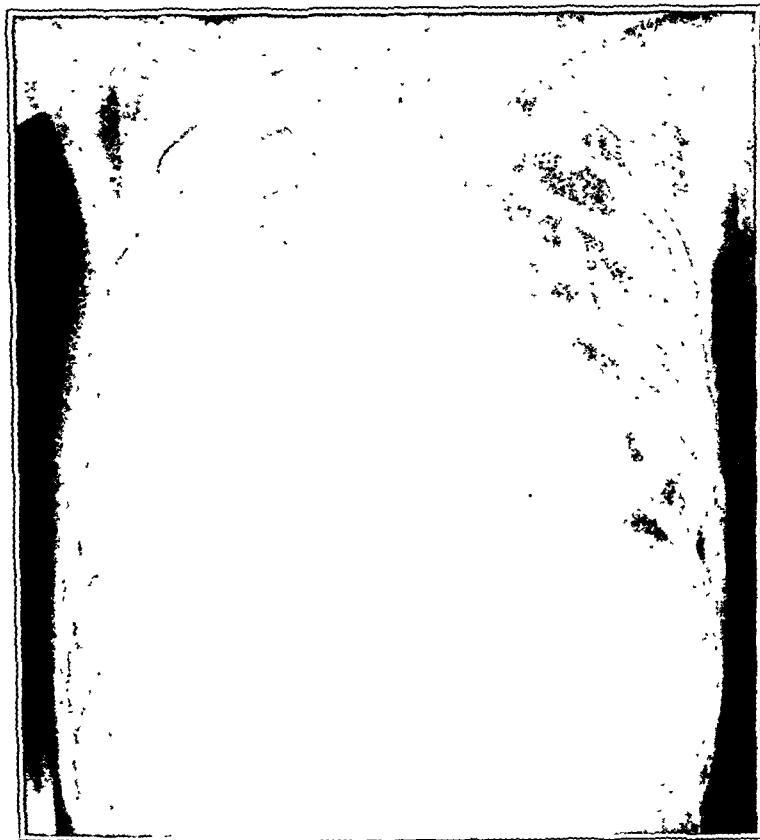


FIGURE 2.

DR. MILFORD SCHULZ: The film of the chest taken shortly after entry shows a densely consolidated area in the lower part of the right lung, in which there apparently is an abscess cavity. The miliary process throughout the lungs did not change much during her stay, but the whole right lung became denser, as recorded. It is curious that the bronchi within the consolidated lung contain air. The lung apparently was "drowned." The cavity is not apparent on the second film.

DR. ROPES: We have then two major processes — a severe ulcerative disease of the colon and a pulmonary lesion consisting of a miliary process, marked consolidation and probably cavitation. In addition, I believe that the cardiac findings indicate

although it must be considered. Evidence of other systemic involvement is apparent. Hepatic dysfunction is indicated by several findings — the elevated van den Bergh, the high prothrombin time and the definite, although not marked, abnormality of the serum protein. The clubbing of the fingers could have been secondary to the ulcerative disease in the colon or to the pulmonary disease, possibly accentuated by both. The contractures of the legs are of interest. In general such flexion contractures rarely develop except in the presence of active joint disease or after prolonged immobilization. There was no immobilization in this case, but I hesitate to introduce an element of joint disease.

The case really comes down to the question

to the first, all of which responded promptly to therapy. A proctoscopy revealed a rough bleeding mucosa with many pseudopolyps. Another roentgenogram of the chest on the ninth hospital day (Fig. 2) revealed a marked change, the right lung appearing completely consolidated. Several bronchi in the right lung were seen to contain air, and the miliary process in the left lung had somewhat increased. X-ray examination of the abdomen revealed no evidence of dilated loops; there was enlargement of the spleen, but no definite enlarge-

even at the onset, or soon thereafter, respiratory symptoms were apparent. If the attack of intestinal gripe marked the beginning of the disease, respiratory symptoms appeared at the onset. The first persistent symptom came some two months later and was wrongly diagnosed. The patient had blood in the stools; this was considered of little significance and was thought to have been due to hemorrhoids, which may or may not have been demonstrated. No further attempt was made to find the cause. Since she had diarrhea associated with the blood,



FIGURE 1.

ment of the liver. Examination of the fundi showed venous stasis and slight papilledema but no tubercles or infarcts.

On the thirteenth hospital day, the patient expired.

DIFFERENTIAL DIAGNOSIS

DR. MARIAN ROPES: In this patient of twenty I think it is probably going to be necessary to make two diagnoses, possibly more. Some, or perhaps most, of the anatomic and physiologic changes are relatively apparent, but the etiology is much less obvious. During the first part of the disease the predominant feature was evidence of an ulcerative lesion of the colon. It is significant, however, that

it is even more surprising that no further search was made at that time. Shortly, however, the severity of the disease became apparent, and at the time of her first admission to a hospital the entire picture can be said to have been consistent with idiopathic ulcerative colitis, which appeared to respond rather well to treatment.

The first definitely atypical symptom was the attack of severe pain in the chest. Again, no attempt was made to determine the cause of the pain. It was treated with diathermy and apparently was of short duration. Both the gastrointestinal symptoms and the respiratory symptoms increased steadily, however, and at the time of the second admission to the outside hospital she had, in addition to a

The joint disease is of interest. About 10 per cent of patients with ulcerative colitis have rheumatoid arthritis. It is an important finding, since it complicates treatment.

This case was hopeless from the beginning, but it seemed to me that we had to give her the benefit of the doubt and try to approach the problem from the point of view of potential colectomy. She was too serious a risk to tolerate major surgery. She died of pulmonary disease, accompanied by active colitis. I do not know anything about coccidiosis of the bowel. I suppose it can occur, but I have never seen a case. I am inclined to doubt that this was a case of coccidiosis of the lung and bowel.

DR. ROPES: Did she have severe diarrhea in the hospital?

DR. JONES: She had constant rectal discharge part of the time, but it let up. We have seen that with extensive involvement of the entire bowel. I was impressed that she did not have marked spasm of the abdominal wall.

DR. LELAND S. MCKITTRICK: Dr. Jones mentioned the possibility and hope of a colectomy in this woman. This has been done in a certain number of desperately ill patients with success. Dr. Daniel F. Jones taught years ago that, if one is able surgically to remove the cause of the illness, the desperately sick patient will tolerate major surgery. In ulcerative colitis one of the basic principles in following out that dictum is the elimination of other conditions or complications, so that when colectomy is done the factor that has been making the patient sick is removed. When the lung condition became apparent in this patient, no attempt was made to remove the colon.

CLINICAL DIAGNOSES

Chronic ulcerative colitis.

Pulmonary tuberculosis?

DR. ROPES'S DIAGNOSES

Granulomatous disease of lungs (? coccidiosis, ? tuberculosis).

Ulcerative colitis (? coccidiosis, ? tuberculosis, ? idiopathic).

Rheumatic heart disease, with mitral involvement.

ANATOMICAL DIAGNOSES

Pulmonary tuberculosis.

Miliary tuberculosis: lung, spleen, liver and kidneys.

Tuberculous peritonitis.

Chronic ulcerative colitis, idiopathic.

Rheumatic heart disease, with mitral stenosis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this woman showed a diffuse process involving the entire colon up to the ileocecal valve; it was characteristic of the healing stage of idiopathic chronic ulcerative colitis. There were, as Dr. Jones mentioned, pseudopolyps with attempted bridging of the mucosa over the previously ulcerated areas. We found no evidence of acute ulcers in the colon; we took about a dozen sections and I could not find a really good ulcer, the epithelium having regrown over the ulcerations. The mucosa, submucosa and muscularis of the bowel showed nonspecific chronic inflammation but no evidence of any other process. The serosa of the bowel, both large and small, was studded with tubercles, so that there was a diffuse tuberculous peritonitis without ascites, which perhaps accounted for the pain and tenderness, as well as the slough around the ileostomy. The process in the lungs was due to active tuberculosis, and there was a miliary spread involving practically every organ of the body. I do not believe that there was any etiologic relation between the ulcerative colitis and the tuberculosis; that is, she had two separate diseases. I am confident that, if she had not developed tuberculosis, the ulcerative colitis could have been cured by colectomy, because it was not so severe a grade of colitis as we often see. Dr. Jones has asked me to hazard a guess concerning when the miliary spread started. I really do not know, but it might have been at the time she developed pain in the chest, about five months before admission.

DR. JONES: What did the heart show?

DR. CASTLEMAN: There was definite old rheumatic involvement of the mitral valve, with a moderate degree of stenosis but no evidence of activity.

A PHYSICIAN: It might be worth while to mention that during the two weeks in this hospital there was practically no discharge from the rectum.

DR. CASTLEMAN: That would fit in with our findings in the colon.

DR. MCKITTRICK: I should like to add a comment to what Dr. Jones said; that is, one cannot depend on the absence of rectal discharge or of diarrhea as evidence of a quiescent ulcerative colitis. I recently had a patient with a fever of 102 to 103°F. and a hemoglobin of 8 gm. or below over a period of weeks who had one formed, guaiac-negative movement a day. Ileostomy and later colectomy were necessary to cure the patient. What Dr. Jones says is correct. The essential thing is to exclude evidence of anything else that can cause fever, debility, anemia and so forth.

The house staff is to be congratulated for finding this pulmonary condition. It looks obvious in the x-ray films, but when you saw this young woman it was a different story.

whether the pulmonary lesion and the ulcerative disease of the colon were due to the same etiologic agent, and if they were, what was the agent. The possibility that malignant disease was the explanation of this entire picture is extremely unlikely. On the other hand, various types of infection ought to be considered. One that is likely to give lesions of this type is tuberculosis. There are many unusual features, however. If the disease was primary in the lungs, which one must assume, the early onset of relatively severe colitis is unusual. The co-existence of a miliary process during the period of marked progression of the consolidation of the lobes is also atypical. Furthermore, the failure to find organisms is most unusual, although not impossible. Unfortunately, we are told the result of only one sputum examination. Possibly the patient did not raise sputum at any other time; but that is definitely unlikely because we know that early in the course of the disease she was raising sputum. The blood-cell counts and the differential are consistent with tuberculosis, but do not aid greatly in making the diagnosis. If the colitis was due to tuberculosis I should not expect a marked improvement during the early stage, with severe colitis thereafter. Again, this does not rule tuberculosis out, but it is unusual.

The possibility of parasitic infection must be considered, but I am unable to think of a parasitic or fungus infection to explain the whole picture. The one diagnosis that should possibly be considered is coccidiosis. The patient came from Oklahoma, which is included in the region where coccidiosis has been seen quite frequently. Coccidiosis can explain pulmonary lesions of this type. As I came into the room I asked Dr. Chester Jones whether he had heard of coccidiosis associated with ulcerative colitis. He said that he had not, but I wonder if this is one of the cases of diffuse involvement that are occasionally seen in this disease. The liver disease here might be ascribed to that.

In summing up the situation I shall conclude that the pulmonary lesions and the ulcerative disease of the colon were probably related. I expect that granulomatous lesions were found, perhaps not due to tuberculosis but possibly, although not likely, due to coccidiosis. Idiopathic ulcerative colitis in addition to the pulmonary disease is a possibility. I also believe that the patient had rheumatic heart disease with mitral involvement.

DR. CHESTER M. JONES: I saw this patient in the outside hospital before she was transferred here. She was a desperately sick woman at that time, and it was obvious that the chances of recovery were extremely slight. She had an ulcerative colitis that had progressed rapidly in spite of ileostomy, presumably done at the proper time. In addition she still had evidence of active ulcerative colitis, as indicated by diarrhea. She was markedly undernourished and greatly depleted, even after intensive treatment. We tried to cover the obvious deficien-

cies in various ways — vitamins, protein and so forth. The ileostomy was functioning but was surrounded by a sloughing area.

At that time the pulmonary situation was not apparent. My belief was that she probably had an idiopathic ulcerative colitis, because of the rather characteristic course. It started out as a relatively mild affair, with exacerbations and remissions, and then became much worse under conditions that were favorable for its progress. She was an extremely apprehensive person. She had been separated from her husband part of the time and the whole situation was difficult for her. Such a psychic background is a factor in ulcerative colitis and must always be taken into account.

When I examined her, there was tenderness in the flank, with slight rigidity. I thought that there was marked cellulitis of the bowel wall and was afraid that there might have been perforation. The prognosis appeared hopeless unless it was possible to take out the diseased colon, a major problem that could be done only as a desperate final move.

The experience with penicillin is of interest. During the last two years we have found that penicillin is of practically no value in ulcerative colitis. In one case that I have seen there was a brilliant result from its use, but in other cases there has been no favorable response.

The clubbing of the fingers was not unusual for this grade of chronic diarrhea, as Dr. Ropes has pointed out, although the mechanism of its production is not understood. The prolongation of prothrombin time is another common finding in serious diarrhea. We have seen two or three cases of infection in the liver itself as a result of ulcerative colitis, but it is rare. Enlargement of the spleen is not uncommon.

One point cannot be too heavily stressed: the treatment of hemorrhoids because of rectal bleeding without an adequate investigation must be avoided. I believe the rule still holds on the surgical service that a hemorrhoidectomy for bleeding is not permitted until sigmoidoscopy is done. Is that correct, Dr. Allen?

DR. ARTHUR W. ALLEN: Yes.

DR. JONES: That is a tremendously important dictum. This woman was treated for hemorrhoids because of the bleeding, when, as a matter of fact, the bleeding was due to ulcerative colitis. Experience has taught us that any local treatment tends to light up the disease.

I should doubt very much that these ulcers were tuberculous. The ulcerations of tuberculous colitis are usually sluggish, punched-out lesions with undermined edges. If one saw them in the rectum it would mean extensive disease, and in a severely ill patient one would expect the ulcerations to be typical. Here, apparently they were not. There was a large area of mucosa covered with pseudopolyps, with characteristic bleeding.

The joint disease is of interest. About 10 per cent of patients with ulcerative colitis have rheumatoid arthritis. It is an important finding, since it complicates treatment.

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1945

THE year of decision that was 1944 has joined the procession of the past, and the year of decision 1945 becomes our present and immediate future. Again we are faced with the promise of a credit of days to be put to use before the current annual allotment expires, and again we are confronted with certain goals that we hope to attain before the new year becomes another old one.

The year 1944, although one of decision, was certainly not our year of fulfillment. In 1944, it is true, we launched mighty offensives on land and sea, but the final decision is not yet in sight, and we have come to a realization of other facts associated with our great effort, to an appreciation of the possibility that war can bring us the extremes in human con-

duct—great sacrifices and great suffering on the one hand, and great selfishness and great indulgence on the other.

At a period when millions of our countrymen are putting in jeopardy their chief possession, and casualty lists are mounting, many thousands of others are maneuvering for a greater share of the restricted necessities of life, are bargaining for ignoble luxuries, are deserting essential industries and are strangers to that spirit of sacrifice without which a cause cannot be wholly won.

We will learn, in the year that we are entering, some useful and some chastening lessons. We will come with reluctance to a full appreciation of the fact that we are engaged in the most momentous and the bloodiest war of our history. We will realize, after three years in arms, that the early warnings of the experts were well founded, and that this time there is no easy road to victory, no slick trick by which the days of peace can be restored to us. We will be taught, perhaps in this year and certainly in the years to come, that the ending of war may bring practically anything but peace, for there can be no peace with cruelty, hatred and evil, or while there is still anything to fight for.

We will learn, by an experience that living generations have never yet encountered, that when a democracy goes to war it can win only with the full support of its people, that every individual must participate and that the extent and the speed of the victory are determined by the effort that is made. We may hope also that those in authority will finally learn that it pays to keep faith with the public, that in the long run truth pays better dividends than does propaganda and that any partnership must be based on mutual confidence.

Certain words of Paul to the Corinthians may be taken to heart also by all Americans, "He which soweth sparingly shall reap also sparingly; and he which soweth bountifully shall reap also bountifully."

CHEMOTHERAPY OF TUBERCULOSIS

TUBERCULOSIS is one of the diseases that is usually considered as not being responsive to sulfonamide drugs. At present it is also being listed among the

conditions in which penicillin is ineffective. Because of the nature of this infection and its great prevalence, it is easy to understand why the lay press continually plays up any encouraging news concerning agents that possibly have a curative effect in the disease. If, however, such agents must be used for a long time and under conditions that are themselves not without danger to the health and life of the patient, such unwarranted publicity may cause considerable harm.

Many physicians throughout this country, particularly those interested in pulmonary diseases, have been considerably annoyed in recent months by the publicity given to one of the newer chemotherapeutic agents that is now being investigated in experimental tuberculosis and in human clinical cases. Indeed, the members of the American Trudeau Society, a group of eminent physicians with particular interest in the treatment of pulmonary tuberculosis, have considered this matter to be serious enough to warrant a special report by its Committee on Therapy. This report, which was presented at a meeting of the Medical Section of the National Tuberculosis Association on March 17 and 18, 1944, was published in the April issue of the *American Review of Tuberculosis*. It should serve to clarify the position of experts concerning the present status of the therapeutic agents under investigation. The following is quoted from this report:

It is the opinion of the committee that the clinical and roentgenological data so far made available to the committee on the action of Diasone on human tuberculosis are as yet inadequate, both quantitatively and qualitatively, to permit, even tentatively, a positive evaluation of its curative effects upon tuberculosis in humans. The committee believes that there is, at this time, no adequate basis for the optimistic implications of the magazine articles or of the releases to the press which are now so well known to both the profession and public. It is believed, on the contrary, that such implications are distinctly unwarranted and not in accord with the clinical evidence which has been reviewed by the committee. The committee regrets exceedingly that the magazine articles mentioned previously were published in spite of efforts on the part of both the committee and the clinician to stop their publication.

Until controlled studies of a definite scope have been reported, it is recommended that none of these drugs be used for treating tuberculous patients except under conditions which will appreciably add to our knowledge of their clinical action, and in the presence of adequate facilities to protect patients effectively from their potentially serious toxic

Patients and physicians must also be

reminded of the provisions of the federal regulations which prohibit the distribution of a drug in the experimental phase of development to other than research institutions to which the material is assigned by the manufacturer for either laboratory or clinical investigation. The committee is informed that other clinical investigations are now in progress, and it is the expressed opinion of the committee that such further well-controlled clinical investigation is distinctly desirable.

Any use of chemotherapeutic agents, including Diasone, in the treatment of tuberculous patients, must, therefore, be regarded as purely a project in clinical investigation. It must be again emphasized that such use is not without hazard and that the roentgenological and clinical evidence reviewed by the committee gives no justification at this time for any attitude concerning the value of these drugs in patients other than one of critical interest.

It is of interest that the same issue of the *American Review of Tuberculosis* contains a paper by Petter and Prenzlau, entitled "Treatment of Tuberculosis with Diasone," which was presented before the Mississippi Valley Trudeau Society in September, 1943. It is followed by a discussion by Dr. C. H. Hinshaw, who, interestingly enough, is the chairman of the Committee of Therapy of the American Trudeau Society. In his remarks, Dr. Hinshaw mentions several reports from Great Britain and the United States that suggest that Promin, another and similar chemotherapeutic agent, may have some therapeutic value. These reports, he adds, are encouraging, but he emphasizes that conclusive proof of efficacy in clinical tuberculosis is lacking for both Promin and Diasone. He also calls attention to the unpredictability of tuberculosis and to its marked tendency to heal without treatment, both of which, to be excluded, require rigid control. He also mentions studies carried out at the Mayo Foundation, which indicate that Diasone is less effective than Promin in experimental tuberculosis in guinea pigs. The Mayo workers also have found that both these drugs are more toxic to human beings than to guinea pigs. These toxic effects may be disturbing and even alarming, although they are usually controllable, unless there is an idiosyncrasy, by properly regulating the dosage. The slow rate of excretion of these drugs necessitates the greatest care in their use.

Petter and Prenzlau report observations on the use of Diasone in 44 patients with human tuberculosis who received an average of 0.9 gm. daily for an average of one hundred and fifty-six days.

They noted some degree of improvement in all the minimal and moderately advanced cases and in 79 per cent of far-advanced cases. Sputum conversion occurred in 59 per cent of all cases, and cavities closed during treatment in 43 per cent. They discuss the general reactions that were observed and emphasize the need for careful clinical and laboratory observations during the administration of the drugs. They believe that their findings point the way to further advances in the treatment of tuberculosis in man.

In a discussion in the May '26 issue of *Science*, under the title "The Paper Shortage and Scientific Publication," Griggs proposes early publication of abstracts or making promptly available in the form of microfilms all scientific papers as soon as they are received for publication. This, he feels, would serve the important purpose of acquainting scientists regarding the results of research by fellow workers. This, in turn, would help them in the conduct of their own studies and would have a tendency to reduce duplication of effort. So far as this discussion concerns scientific journals as a means of keeping research workers informed, there is much to be said in favor of these proposals.

Griggs goes on to stress the contributions of such abstracting magazines as the *Reader's Digest* to the field of literature. There is much to be said in favor of this argument. This type of magazine and other lay magazines may, in addition, render a useful service in popularizing some of the leading medical and scientific advances. It may not be entirely safe or desirable, however, to entrust these lay magazines with the premature announcement of great scientific discoveries in the field of medicine. Their function could best be served only after adequate and thorough discussion of the value of these discoveries by competent investigators in the field has proved beyond a doubt the value of the discoveries that they wish to popularize.

It is highly desirable that, in the future, such magazines try to avoid doing the disservice that has, in the past, resulted from rosy pictures prematurely painted concerning proposed remedies that are only in the process of being clinically evaluated. Such publication later results in serious disillusionment to the afflicted persons who seek relief, and not in-

frequently adds to their suffering, in addition the considerable expense to which they may put in the process.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

GRIMES — Warren P. Grimes, M.D., of Hillsboro died November 13. He was in his seventy-seventh year. Dr. Grimes received his degree from Harvard Medical School in 1891. He was a member of the New Hampshire Medical Society and the American Medical Association. His widow survives.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	January 3	William T. Green
Lowell	January 5	Albert H. Brewster
Salem	January 8*	Paul W. Hugenberger
Brockton	January 11	George W. Van Gorp
Pittsfield	January 15	Frank A. Slowick
Springfield	January 17	Garry deN. Hough
Worcester	January 19	John W. O'Meara
Hyannis	January 23	Paul L. Norton
Fall River	January 29*	Eugene A. McCarthy

*Day changed.

NOTICES

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the of the New England Hospital for Women and Children be held on Thursday, January 4, at 7:15 p.m., in the room of the nurses' residence. Dr. Miriam G. Katzeff speak on the subject "Postmenopausal Osteoporosis."

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINN THURSDAY, JANUARY 4

FRIDAY, JANUARY 5

*9:00-10:00 a.m. Cancer of the Cervix. Dr. B. Lorincz. Joseph Pratt Diagnostic Hospital.

10:50 a.m. Benign New Growth. Dr. E. Lafreniere. (Postgraduate clinic in dermatology and syphilis.) Dowling Amphitheater Boston City Hospital.

12:00 m.-1:00 p.m. Clinicopathological conference. Boston Floating Hospital. Held in Lecture Hall of Joseph H. Pratt Diagnostic Hospital.

SATURDAY, JANUARY 6

*10:00 a.m.-12:00 m. Medical staff rounds. Peter Bent Brigham Hospital

MONDAY, JANUARY 8

12:00 m.-1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital

TUESDAY, JANUARY 9

*12:15-1:15 p.m. Clinicoröntgenological conference. Peter Bent Brigham Hospital

(Notices continued on page xvii)

